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Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

CITIZEN PETITION

Vaccine For All LLC hereby submits this petition under 21 C.F.R. §10.30 to request that the Commissioner of Food and Drugs amend 21 C.F.R. §312.

With this petition, Vaccine For All seeks the creation of a new Food and Drug Administration policy to achieve expanded and accelerated development and production of pre-pandemic and pandemic vaccine. Research has shown, as detailed in Part B, that vaccination with pre-pandemic vaccine could: 1) potentially save the lives of those vaccinated; 2) double the number who can be vaccinated with limited early supplies of pandemic vaccine; and 3) limit the extent of a pandemic, as those vaccinated fight infection more effectively and thus limit contagion. Expanded production capacity developed to produce pre-pandemic vaccine could be used, in the event of a pandemic, to more rapidly produce pandemic vaccine. Thus, public health is best served by expanding production of pre-pandemic and pandemic vaccine, and enabling all who desire vaccine to obtain it.

Specifically, the requested policy would explicitly permit a sponsor, which had received FDA approval to begin Phase I clinical trials for a pre-pandemic or pandemic vaccine, to market and sell *best efforts* to produce and deliver FDA-approved pre-pandemic or pandemic vaccine (Best Efforts). If the sponsor earned FDA marketing approval for the vaccine, the sponsor would deliver the vaccine; otherwise, it would not deliver vaccine.

This policy would not alter the requirement to earn FDA marketing approval before distributing vaccine. Yet it would permit individuals, families, employers, and other entities to finance research, development, production capacity and production of pre-pandemic and pandemic vaccine. To the extent such vaccine earns FDA approval and is distributed, it would save lives in the event of a pandemic (as shown by research described below under Part B, "Policy rationale").

In selling Best Efforts, a sponsor would specify the total amount of funds it would seek to raise in the sale, and how it would allocate those funds to research, development, production capacity and production. A sponsor could cancel any sale of Best Efforts if it were not fully subscribed

(e.g., if the sale proceeds would be insufficient to fund the planned expenditures). To ensure that a sponsor, after selling Best Efforts, has an appropriate financial incentive to diligently pursue FDA marketing approval, the policy would require a second payment upon delivery of FDA-approved vaccine.

To expand production of vaccine through the sale of Best Efforts, Vaccine For All also seeks an explicit FDA policy to permit those who purchase Best Efforts to purchase additional Best Efforts and donate any resulting FDA-approved vaccine to government or to a charity registered under section 501(c)(3) of the Internal Revenue Code, with no second payment. Purchase of additional Best Efforts could be incorporated, for example, in an auction or other price-finding mechanism in the sale of Best Efforts. That is, a sponsor could first sell Best Efforts to those parties that were willing to make a linked purchase of additional Best Efforts and donate any resulting FDA-approved vaccine.

As further detailed in Part B below, our analysis of the Food and Drug Administration's statutory authority indicates that this proposal would fully comport with the Food, Drug, and Cosmetic Act of 1962, as amended. We believe this measure is needed to finance expanded and accelerated production of pre-pandemic and pandemic vaccine, to provide for pandemic preparedness and public health.

A. ACTION REQUESTED

The FDA has implemented its statutory authority over testing of investigational drugs with the regulatory scheme set out in 21 C.F.R. §312. The provisions that should be amended are set out below, with the text of the requested amendments shown in bold type.

Sec. 312.7 Promotion and charging for investigational drugs

(a) *Promotion of an investigational new drug.* A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution. **Notwithstanding the foregoing or any other provision of this section, any sponsor or any person acting on a sponsor's behalf, once the FDA has approved the sponsor's pre-pandemic or pandemic vaccine candidate to begin Phase 1 trials and in advance of the sponsor receiving FDA marketing approval, may promote, market, commercialize and sell, to any person, best efforts to produce and deliver FDA-approved pre-pandemic or pandemic vaccine, without needing FDA approval for any marketing materials, where: 1) a pre-pandemic or pandemic vaccine is defined to include any H5N1 vaccine and any other vaccine to protect against an infectious disease with a case fatality rate of five percent or greater, as determined by World Health Organization statistics; 2) purchasers of best efforts may include, without limitation, an individual, a family, an employer purchasing**

best efforts for its staff, an insurance company purchasing best efforts for its insured parties, and an association, church, or other entity purchasing best efforts for its members; 3) when a sponsor or any person acting on a sponsor's behalf sells best efforts, and the sponsor later earns FDA marketing approval, the sponsor or person acting on the sponsor's behalf may deliver vaccine to purchasers of best efforts only upon receipt of a second payment in an amount specified at the time of the best efforts payment, and which is at least one-third the amount of the best efforts payment; and 4) a sponsor or any person acting on a sponsor's behalf may sell, to those who purchase best efforts, additional best efforts for additional vaccine for donation, as designated by the purchaser, to the federal government, a state or local government, or a charity registered under section 501(c)(3) of the Internal Revenue Code, and after doing so, if the vaccine earns FDA marketing approval, the sponsor or person acting on the sponsor's behalf must donate the additional vaccine that results as designated by the purchaser of best efforts, without any second payment.

(b) *Commercial distribution of an investigational new drug.* A sponsor or investigator shall not commercially distribute or test market an investigational new drug. **This limitation does not apply to marketing and sale of best efforts to produce and deliver FDA-approved pre-pandemic or pandemic vaccine under 312.7(a).**

(c) *Prolonging an investigation.* A sponsor shall not unduly prolong an investigation after finding that the results of the investigation appear to establish sufficient data to support a marketing application.

(d) *Charging for and commercialization of investigational drugs*--(1) *Clinical trials under an IND.* Charging for an investigational drug in a clinical trial under an IND is not permitted without the prior written approval of FDA. In requesting such approval, the sponsor shall provide a full written explanation of why charging is necessary in order for the sponsor to undertake or continue the clinical trial, e.g., why distribution of the drug to test subjects should not be considered part of the normal cost of doing business. **This limitation does not apply to marketing and sale of best efforts to produce and deliver FDA-approved pre-pandemic or pandemic vaccine under 312.7(a).**

(2) *Treatment protocol or treatment IND.* A sponsor or investigator may charge for an investigational drug for a treatment use under a treatment protocol or treatment IND provided: (i) There is adequate enrollment in the ongoing clinical investigations under the authorized IND; (ii) charging does not constitute commercial marketing of a new drug for which a marketing application has not been approved; (iii) the drug is not being commercially promoted or advertised; and (iv) the sponsor of the drug is actively pursuing marketing approval with due diligence. FDA must be notified in writing in advance of commencing any such charges, in an information amendment submitted under 312.31. Authorization for charging goes into effect automatically 30 days after receipt by FDA of the information amendment, unless the sponsor is notified to the contrary. **This limitation does not apply to marketing and sale of best efforts to produce and deliver FDA-approved pre-pandemic or pandemic vaccine under 312.7(a).**

(3) *Noncommercialization of investigational drug.* Under this section, the sponsor may not commercialize an investigational drug by charging a price larger than that necessary to recover costs of manufacture, research, development, and handling of the investigational drug. **This limitation does not apply to marketing and sale of best efforts to produce and deliver FDA-approved pre-pandemic or pandemic vaccine under 312.7(a).**

(4) *Withdrawal of authorization.* Authorization to charge for an investigational drug under this section may be withdrawn by FDA if the agency finds that the conditions underlying the authorization are no longer satisfied. **This limitation does not apply to marketing and sale of best efforts to produce and deliver FDA-approved pre-pandemic or pandemic vaccine under 312.7(a).**

B. STATEMENT OF GROUNDS

Policy rationale: According to World Health Organization (WHO) data, bird flu kills more than half of those people infected, sparing no age groups. Thus, if a bird flu pandemic emerges, all would need vaccine. A WHO report concluded that if bird flu evolves to trigger a pandemic, it could maintain its current 50-percent-plus case fatality rate (WHO, "Influenza Research at the Human and Animal Interface," September 2006). In a pandemic, exposure to a virulent, highly lethal virus without protection from vaccine could result in the deaths of millions of Americans. Yet the current global capacity to produce pre-pandemic or pandemic vaccine would cover only a small fraction of the global population. The U.S. Government currently plans to purchase 20 million courses of pre-pandemic vaccine, which would leave 280 million Americans initially unprotected in the event of a pandemic. The U.S. Government seeks the capacity to obtain pandemic vaccine for all Americans within six months of any pandemic outbreak, but even after we achieve this capacity millions could die in the first six months.

A policy explicitly permitting the marketing and sale of *best efforts* to produce and deliver FDA-approved pre-pandemic or pandemic vaccine (Best Efforts) would enable individuals, families, employers and other entities to finance expanded and accelerated development and production of pre-pandemic and pandemic vaccine. The requirement to earn FDA marketing approval before distributing vaccine would not be altered.

The need for expanded and accelerated production of pre-pandemic vaccine is shown by the following:

1. Pre-pandemic vaccine could potentially save lives, as shown in an animal study: Ferrets—animals whose response to vaccine is most similar to that of humans—vaccinated with an earlier strain of H5N1 bird flu vaccine survived a challenge infection with a more recent strain. (Govorkova, Elena A., et al., "Efficacy of H5N1 Vaccine in Ferrets," *Journal of Infectious Diseases* 2006:194 (15 July), pp. 159-167.)

2. Pre-pandemic vaccinations could double the number who could be vaccinated with limited early supplies of pandemic vaccine: Vaccinating humans with a "priming" vaccination targeted to an early strain of H5N1 can make effective a single "booster" dose of an H5N1 vaccine targeted to a newer strain (where two doses of the newer vaccine would otherwise be needed)—

indicating that pre-vaccination with pre-pandemic vaccine could double the number of people whose lives could be saved with limited early supplies of pandemic vaccine. (Goji, Nega Ali, et al., "Immune Responses of Healthy Subjects to a Single Dose of Intramuscular Inactivated Influenza A/Vietnam/1203/2004 (H5N1) Vaccine After Priming with an Antigenic Variant," presentation at the Infectious Diseases Society of America annual meeting, Oct. 12-15, 2006.)

3. Pre-pandemic vaccinations could limit the extent of a pandemic: Every person who is vaccinated would, in the event of a pandemic, fight infection more effectively and thus limit contagion. For example, research modeling the effectiveness of widespread vaccination with a low-efficacy vaccine (e.g., a pre-pandemic vaccine) found that for a moderately contagious virus, social distancing plus the low-efficacy vaccine limited cases to only a few per thousand. (Germann, Timothy, et al., *Proceedings of the National Academy of Sciences*, April 11, 2006, Vol. 103, No. 15, pp. 5935-5940.)

4. Governments are stockpiling pre-pandemic vaccine: Recognizing the public health value of pre-pandemic vaccine, as noted in items 1-3 above, the U.S. Government and other national governments (e.g., in Europe) are stockpiling pre-pandemic vaccine.

5. "Surge capacity" is needed to produce vaccine for all in the event of a pandemic: Expanded production capacity developed to produce pre-pandemic vaccine could be used, in the event of a pandemic, to more rapidly produce adequate supplies of pandemic vaccine.

The advantages of this proposed policy are as follows:

1. The requirement to earn FDA marketing approval before distributing vaccine would not be altered: Firms that sold Best Efforts could deliver vaccine only if the vaccine earned FDA marketing approval; otherwise they could not deliver vaccine.

2. Demand for pre-pandemic vaccine and potential supply of Best Efforts already exist—only a regulatory change is needed to achieve private financing of expanded vaccine capacity: The potentially significant demand for Best Efforts is indicated by an AP/Ipsos poll (April 21, 2006) which found that one-third of Americans—or one hundred million Americans—are concerned that someone in their family could fall ill with bird flu, and that one-half believe that if they fell ill with bird flu they would die. The poll also found that a strong majority favor access to vaccine or antiviral drugs. A potentially significant supply of Best Efforts has been identified by Vaccine For All through its preliminary communications with biotechnology and pharmaceutical firms developing H5N1 vaccine.

3. Without this policy, there will be less investment in pre-pandemic and pandemic vaccine, and slower development of vaccines and production capacity: Without the advance payments to vaccine developers for research, development, production capacity, and production that this policy would achieve (beyond those payments being made by government to some vaccine developers), and without shifting of the risk of failure to earn FDA approval from vaccine developers to vaccine purchasers, vaccine developers will invest less in pre-pandemic and pandemic vaccine, thus slowing development of safe and effective vaccines and vaccine production capacity.

4. Purchasers would be protected from purchasing Best Efforts where the likelihood that the sponsor's vaccine will earn FDA approval is too remote: To protect consumers from purchasing Best Efforts where the sponsor's likelihood of earning FDA marketing approval is too remote, only sponsors that have earned the right to begin Phase 1 clinical trials, and persons acting on such sponsors' behalf, would be permitted to sell Best Efforts.

5. Vaccine producers would be protected if their good faith efforts to earn FDA approval were unsuccessful: To protect vaccine developers who engage in good faith Best Efforts by investing Best Efforts payments in vaccine research, development, production capacity, and production, Best Efforts payments would not be refunded in the event the sponsor does not earn FDA marketing approval. (This need not be specified in the regulation because this would be specified in any best efforts contract.)

6. Permitting the sale of additional Best Efforts would facilitate the sale of sufficient Best Efforts to finance the required level of investment by vaccine developers, and would result in donation of any resulting FDA-approved vaccine: Permitting a purchaser of Best Efforts to purchase additional Best Efforts and donate any resulting FDA-approved vaccine to government or to a charity registered under section 501(c)(3) of the Internal Revenue Code will facilitate the collective purchase by individuals, families, employers, insurance firms, churches, associations and other entities of Best Efforts in sufficient quantity to finance the required investments by vaccine developers. To the extent that the purchase of Best Efforts results in FDA-approved vaccine, the purchase of additional Best Efforts will also result in donations of FDA-approved vaccine to government, at no cost to taxpayers, and to registered charities, which may deliver the vaccine in regions of the world that are likely bird flu outbreak areas, thus helping prevent a pandemic from emerging.

7. A second payment upon delivery of FDA-approved vaccine would provide a further incentive to apply for FDA marketing approval: Linking the sale of Best Efforts to a second payment of at least one-third the Best Efforts payment, if and when FDA-approved vaccine is delivered, provides an appropriate financial incentive to induce a sponsor to complete clinical trials and file for FDA marketing approval. Specifying the amount of the second payment at the time of the Best Efforts payment protects consumers from an unduly high second payment in the event that a pandemic emerges. Specifying that there will be no second payments for donated vaccine ensures that no government or charity outlays are needed to accept donated vaccine.

Statutory authority: Our proposed policy is not inconsistent with the Federal Food, Drug, and Cosmetic Act, which states in relevant part (Sec. 505 [21 U.S.C. 355]): "(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug." Our proposed policy involves only the sale and marketing of Best Efforts, and would not permit introduction into interstate commerce any vaccine until it is FDA-approved.

C. ENVIRONMENTAL IMPACT

Petitioner claims a categorical exclusion under 21 C.F.R. §25.30(h).

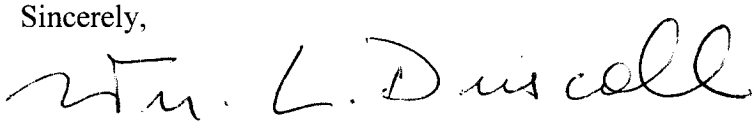
D. ECONOMIC IMPACT

Petitioner believes that: 1) the proposed policy would result in a higher rate of vaccination among the population against a potential influenza pandemic; and 2) this higher rate of vaccination would, in the event of a pandemic, limit infection, contagion, morbidity, and mortality, thus reducing the economic impact of the pandemic—i.e., the proposed policy would have a positive economic impact. Petitioner will submit further information and analysis regarding economic impact upon request of the Commissioner.

E. CERTIFICATION

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Sincerely,



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Cc: Dr. Andrew von Eschenbach, Commissioner of Food and Drugs

Three copies of Citizen Petition From Vaccine For All LLC, to request that the Commissioner of Food and Drugs amend 21 C.F.R. section 312, received today.

Pike Expedition, November 1806, Rocky Mountains

Vaccine For All
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