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200 Park Avenue, 17th Floor, New York, NY 10166
sirillp.com | P: (212) 532-1091 | F: (646) 417-5967

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VIA EMAIL AND FEDEX

Rochelle Walensky
Director, CDC
Roybal Building 21, Rm 12000
1600 Clifton Rd
Atlanta, GA 30333
Aux7@cdc.gov

Xavier Becerra
Secretary, Health & Human Services
200 Independence Avenue S.W.
Washington, D.C. 20201
c/o Sean McCluskie
sean.mccluskie@hhs.gov

Grace Lee, M.D.
Chair, ACIP
Center for Academic Medicine
Pediatric Infectious Diseases, Mail Code: 5660
453 Quarry Road
Stanford, CA 94304
gmlee@stanford.edu

Members,
Advisory Committee on Immunization Practices
acip@cdc.gov

Re: Ticovac, Vaxchora, PreHevbrio, 2022 Influenza vaccines, Priorix, Vaxneuvance

Dear Dr. Walensky, Mr. Becerra, Dr. Lee, and ACIP Members:

The CDC's Advisory Committee on Immunization Practices reviewed data in connection with six vaccines (Ticovac, Vaxchora, PreHevbrio, 2022 Influenza vaccines, Priorix, and Vaxneuvance) at its meeting on February 23 and 24, 2022. We write on behalf of the Informed Consent Action Network ("**ICAN**") to bring to your attention troubling deficiencies in connection with ACIP's reviews of all six vaccines.

As part of our work for ICAN, we assign experts in the field to watch, takes notes, and summarize every ACIP meeting and compare ACIP practices against best practices in science. CDC staff and ACIP members will get the wrong answers if they ask the wrong questions. The result can be recommending a vaccine that does not work very well or, worse, causes significant iatrogenic injury.

In Exhibit A, attached to this letter, you will see a brief critique of the problems with the CDC's existing frameworks: GRADE, PICO, and EtR. In Exhibit B, you will see an appropriate framework that ICAN has developed, TASQ, for evaluating vaccine candidates based on 5 questions that represent best practices in the scientific evaluation of vaccines. In the analysis below, we will use the TASQ framework to guide the evaluation of each vaccine.

I. Ticovac (tickborne encephalitis vaccine)

As the presenter Susan Hills acknowledged, cases of tickborne encephalitis ("**TBE**") in the U.S. are extremely rare – just 20 recorded cases total over the last 20 years.[1]

The CDC did not mention that for most travelers the risk of TBE can be reduced by using insect repellents and protective clothing to prevent tick bites. Furthermore, a recent case study in the Swedish medical journal *Läkartidningen* found that high dose corticosteroids were effective in treating TBE.[2]

Ticovac was apparently not tested in a double-blind randomized placebo-controlled study. The FDA mentions 10 studies but the only control described is "a non-US licensed TBE vaccine comparator."[3]

Even if there had been a proper control group, the sample size of the combined studies was too small. The FDA states, "Among a total of 10 clinical trials, 3,240 healthy children 1 through 15 years of age received at least one dose of TICOVAC. A total of 4,427 healthy adults 16 years of age and older received at least one dose of TICOVAC in 10 clinical trials." Serious adverse events that occur in one in a few thousand children would likely be missed by these trials. By contrast, the clinical trial for the Salk polio vaccine had 1.8 million participants.[4]

According to the FDA, "each 0.5 mL dose of Ticovac is formulated to contain 2.4 microgram (µg) TBE inactivated virus, 0.5 mg human serum albumin, 0.35 mg aluminum hydroxide, 3.45 mg sodium chloride, 0.22 mg dibasic sodium phosphate, and 0.045 mg of monobasic potassium phosphate. From the manufacturing process, each 0.5 mL may also contain formaldehyde (≤5 µg), sucrose (≤15 mg), protamine sulfate (≤0.5 µg), and trace amounts of chick protein and DNA from CEF cells, neomycin and gentamicin."[5] The FDA acknowledges that use of human serum albumin comes with a small risk for transmission of Creutzfeldt-Jakob disease.[6] Aluminum adjuvants are toxic.[7] Some people are allergic to neomycin and gentamicin.

Postmarketing experience in Europe lists a wide range of adverse events following Ticovac including herpes zoster, anaphylactic reactions, demyelinating disorders, visual impairment, tinnitus, and tachycardia to name a few.[8] Due diligence requires that the CDC investigate this troubling data from Europe, estimate the rates of adverse events in countries that have already granted licensure, and estimate the likely degree of undercounting in the reported data.

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[1] *See* https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-23-24/02-TBE-Hills-508.pdf.

[2] *See* https://pubmed.ncbi.nlm.nih.gov/28632298/.

[3] https://www.fda.gov/media/151502/download at p. 5.

[4] *See* https://www.history.com/this-day-in-history/polio-vaccine-trials-begin.

[5] https://www.fda.gov/media/151502/download.

[6] *See* https://www.fda.gov/media/151502/download at p. 3.

[7] See https://www.icandecide.org/wp-content/uploads/2019/09/ICAN-AluminumAdjuvant-Autism.pdf.

[8] *See* https://www.fda.gov/media/151502/download.

The lower bound estimate of the number needed to vaccinate to prevent one case in travelers is 2 million.[9] The upper bound estimate is 30 million. This means that for the benefits to exceed the risks, this vaccine must cause no more than 1 serious adverse event for every 2 million doses. That has never been shown.

Moreover, at $250 a dose, ACIP is proposing to spend $500 million to $7.5 billion to prevent a single *case* of TBE. This is a not an efficient use of funds, including taxpayer funds, that will likely be used to purchase this product. This means the real beneficiary here will be Pfizer, a company that has paid "the largest criminal fine ever imposed in the United States for any matter."[10]

The chances of contracting tickborne encephalitis are so small that the risks of the vaccine outweigh the benefits for everyone except laboratory workers (who may not actually be protected by the vaccine if they are, for example, working on gain-of-function viruses). Given the foregoing, it is astonishing that this vaccine was approved unanimously.

II. Vaxchora (cholera vaccine)

Cholera is so rare in the U.S. that the "Evidence to recommendations summary" slides by Jennifer Collins did not even mention the prevalence. So ICAN looked it up. "In the U.S., the occurrence of cholera is very low (0-5 cases per year) and is usually due to ingestion of contaminated food or international travel."[11]

The CDC in their PICO components claim that the comparison treatment is "no cholera vaccine." This is disingenuous. In fact, cholera is usually treatable with rehydration fluid (oral or IV) and antibiotics. That is why they were able to do challenge trials and not violate regulations that govern human subjects research.

Additionally, the observation period was too short. Solicited adverse reactions were only recorded daily for 7 days following vaccination and apparently unsolicited serious adverse events were accepted for only six months.[12]

Even with a proper control and safety review duration, the sample size in the clinical trial was too small to draw any meaningful conclusions: "A total of 468 children 2 through 17 years of age received one dose of VAXCHORA and 75 received placebo (physiologic saline)."[13]

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[9] *See* https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-23-24/02-TBE-Hills-508.pdf at p. 18.

[10] https://www.justice.gov/opa/pr/justice-department-announces-largest-health-care-fraud-settlement-its-history.

[11] https://www.cdc.gov/cholera/infection-sources.html.

[12] *See* https://www.fda.gov/media/128415/download.

[13] https://www.fda.gov/media/128415/download.

Because this is a live virus vaccine, cholera can be transmitted in stool following vaccination for > 7 days.[14] Indeed 11% have stool shedding.[15] So the vaccine itself could potentially trigger an outbreak of cholera.

The rates of abdominal pain in the clinical trials are troubling: 19% in adults, 38% in adolescents 12 to <18 years old, 27% in kids 6 to <12 years, and 17% in kids 2 to <6.[16]

This is a non-adjuvanted vaccine but, as an attenuated live virus vaccine, it may eventually revert to virulence and cause the very illness that it is designed to prevent.

Relative risk reduction appeared good in the challenge trials – 9% infection rate in the treatment group and 59% infection rate in the control group. However, absolute risk reduction in the U.S. approaches zero because the background rate in the U.S. population is so low. Number needed to vaccinate is undefined.

Given the near zero rate of cholera in the U.S., the availability of effective treatments, the high adverse event rate, the good, but not great, relative risk reduction, and the dangers that come with a live virus vaccine, it is surprising that there were no critical questions and ACIP approved the vaccine unanimously for "children and adolescents aged 2 to 17 years traveling to an area with active cholera transmission."

III. 2022 Influenza Vaccines

Why is ACIP recommending flu vaccines that are only 8% effective against Influenza A and 14% effective against A/H3N2 strains?[17]

The "enhanced" flu vaccines that are given to 80% of people who receive flu vaccines are enhanced with additional adjuvants that significantly increase the adverse event rate. There was no discussion at the ACIP meeting of the enhanced adverse event rate from enhanced flu vaccines. As you may be aware, injuries from the flu vaccine were the most compensated vaccine in the Vaccine Injury Compensation Program, and only a small fraction of actual injuries are ever filed in those programs.

Recommending a shot with the efficacy rates noted above and that causes iatrogenic injury erodes the credibility of the CDC and HHS.

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[14] *See* https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-23-24/02-Cholera-Collins-508.pdf.

[15] *See* https://www.fda.gov/media/128415/download at p. 13.

[16] https://www.fda.gov/media/128415/download.

[17] And why are the slides presented on February 23, 2022 documenting this data from the seven centers in the U.S. Flu VE Network not posted to the ACIP website?

IV. PreHevbrio (Hep B vaccine)

The seven studies summarized by Lt. Commander Mark K. Weng[18] were not double-blind randomized placebo-controlled trials because the comparator was Engerix-B which never should have been licensed because its clinical trial was underpowered, lacked a control group of note, and only reviewed safety for days after injection.[19]

According to the PreHevbrio package insert, "each 1.0 mL dose is formulated to contain 10 mcg hepatitis B surface antigens (S, pre-S1 and pre-S2) adsorbed on aluminum hydroxide [Al(OH)3] as an adjuvant (aluminum content of 0.5 mg/mL)." As explained above, aluminum adjuvants are known neurotoxins.

Adding PreHevbrio as a non-inferior option is not giving healthcare providers and parents more options, it is compounding an earlier error that must be corrected.

V. Priorix (MMR)

The clinical trials of Priorix are meaningless because they were not double-blind randomized placebo-controlled trials. The placebo was usually MMR-II. As we have shared with you previously, the MMR-II vaccine never should have been licensed by the FDA because the clinical trial was too small (only 834 children), was not a double-blind placebo-controlled (no placebo), and was too short (safety was monitored for only 42 days after injection).[20] Further, the rate of adverse events when comparing these two products – Priorix and MMR-II – rather than evidencing safety, should cause concern. Once again, adding another MMR shot will not give providers and parents more options, it will compound an earlier error that must be corrected.

VI. Vaxneuvance (Pneumococcal)

PCV15 protects against only 15 of the 100 types of pneumococcal bacteria. It contains toxic ingredients. It was never tested against a placebo. It appears that in response to pneumococcal vaccination, the pneumococcal bacteria is evolving toward types that evade the vaccine.

According to the package insert, "each 0.5 mL dose [of Vaxneuvance] contains 2.0 mcg each of S. pneumoniae polysaccharide serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F, and 4.0 mcg of polysaccharide serotype 6B, 30 mcg of CRM197 carrier protein, 1.55 mg L-histidine, 1 mg of polysorbate 20, 4.50 mg sodium chloride, and 125 mcg of aluminum as aluminum phosphate adjuvant."[21] Again, aluminum phosphate adjuvant is a known neurotoxin.

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[18] *See* https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-23-24/02-HepWG-weng-508.pdf.

[19] *See* https://www.icandecide.org/wp-content/uploads/2019/09/ICAN-Reply-1.pdf.

[20] *See* https://www.icandecide.org/fda-documents-reveal-mmr-vaccine-should-never-have-been-licensed/.

[21] https://www.fda.gov/media/150819/download.

CDC presenter Ryan Gierke claimed that, "We are not observing any replacement of new types or serotypes." But that's not what the scientific literature says. A 2019 article from Science Daily, summarizing a recent study published in the Lancet, found that:

> Samples were collected both before and after PCV introduction, and the DNA sequences and health data were compared. This makes it possible to determine changes in the bacteria that could affect how well the vaccine protects against the pneumococcus, and whether new strains are emerging that would impact disease severity and ease of treatment.
>
> The researchers discovered 621 genetic strains globally, each associated with one or more coat types. They also saw that the levels of non-vaccine type bacteria rose after the introduction of PCV, showing how bacteria evolve in response to the vaccine.
>
> Professor Keith Klugman, Director of the Pneumonia team at the Bill & Melinda Gates Foundation, said... "we are fighting a battle against evolution of bacterial strains."[22]

Merck also makes a 23-valent pneumococcal vaccine (Pneumovax). So why market a 15-valent vaccine for kids? It turns out that children <2 years old fail to mount an adequate response to the 23-valent adult vaccine. So there are limits to how many strains one can add to this conjugate vaccine – another important facet of this debate that the CDC and ACIP failed to mention.

Conclusion

The public expects that CDC/ACIP will evaluate the data without bias by using the highest standards of scientific excellence. Unfortunately, the frameworks used by CDC/ACIP shroud weak evidence in a fog of often not meaningful bureaucratic buzzwords. This systematically introduces bias and creates a bureaucratic freight train that only goes in one direction: forward to recommendation. CDC/ACIP can and must do better. ICAN is respectfully asking HHS/CDC/ACIP to examine the ways that existing frameworks for evaluating vaccines systematically introduce bias (as explained in Exhibit A). ICAN, after consulting with a wide range of experts in the field, is proposing a revised framework that is closer to scientific best practices (Exhibit B). ICAN is also troubled by the specific deficiencies in the presentations and

[22] https://www.sciencedaily.com/releases/2019/06/190610142019.htm; https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30297-X/fulltext.

deliberations at the ACIP meeting held on February 23 and 24, 2022 as described in this letter. ICAN looks forward to your response to all of the issues raised herein.

Very truly yours

Aaron Siri, Esq.
Elizabeth Brehm, Esq.

Exhibit A

How PICO, GRADE, and EtR frameworks bias the assessment process for new vaccines

There is a large body of literature that shows that pharmaceutical companies bias clinical trials in their favor by intentionally asking the wrong questions.[1] ICAN has observed a similar pattern with CDC and its Advisory Committee on Immunization Practices ("ACIP") which ask the wrong questions when using the PICO, EtR, and GRADE systems to evaluate evidence.

PICO starts with a policy question and then asks:

- Population
- Intervention
- Comparison
- Outcomes

EtR stands for Evidence to Recommendations Framework. It asks 6 questions:

- Public health problem
- Benefits and harms
- Acceptability
- Equity
- Feasibility
- Values
- Resource Use

GRADE looks a bit like a systematic review but it violates scientific norms for how a systematic review should be conducted. "Grade Summary of Findings" tables have 5 columns:

- Certainty assessment (number of studies, study design, risk of bias, inconsistency, indirectness, imprecision, other considerations)
- Number of patients (treatment, control)
- Effect (relative, absolute)
- Certainty
- Importance

These are all nice words, but they are political words, not scientific terms.

In every case, CDC/ACIP take data from the manufacturer (already a problem) and then fit them into a framework of bureaucratic buzzwords that often have no scientific value. This process *obscures* the underlying data (which is usually weak). CDC/ACIP frequently use words including "certainty," "importance," "precision/imprecision," "critical," "high," "moderate," "low," "minimal," "probably," "acceptability," "feasibility," and "balance of consequences" to make decisions. [2] But these are not standard scientific terms.

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[1] Richard Smith, (2005). Medical journals are an extension of the marketing arm of pharmaceutical companies. *PLoS Medicine*, 2(5), 364–366. https://doi.org/10.1371/journal.pmed.0020138.

[2] There is even an entire CDC/ACIP handbook for how to speak this bureaucratic language. https://www.cdc.gov/vaccines/acip/recs/grade/downloads/handbook.pdf.

The public expects CDC/ACIP to engage in scientific best practices. Unfortunately, the CDC/ACIP evaluation frameworks introduce bias that favors manufacturers and hurts the public interest. The CDC/ACIP evaluation frameworks create the false appearance of scientific rigor regardless of the data. In practice, this means that ACIP almost always recommends a vaccine even where there is little benefit and/or the harms are extraordinary.

Exhibit B

Introducing TASQ, The Appropriate Scientific Questions
5 Scientific Questions for Evaluating Vaccine Candidates

ICAN has developed a set of five scientific questions to evaluate every vaccine. These questions elicit the fundamental safety and efficacy information necessary to properly evaluate each vaccine. The answers are usually knowable and straightforward. Using these five questions will increase transparency, improve public health, and reduce iatrogenic injury.

1. What is known about the **pathogen**? What are the harms (e.g., a rash or something more serious)? What is the rate of harms from this pathogen in the target population?

2. What are the **existing treatments**? What other prevention options exist?

3. Was the vaccine **adequately tested** in a **double-blind, randomized, placebo-controlled trial?** If the answer is no because the control was another vaccine, then was the vaccine used as a control tested in a **double-blind, randomized, properly powered, placebo-controlled trial?** If no, the vaccine should not be recommended for any use. Within the trial:

   a. How long was the **safety review period** after injection for non-minor adverse events? If less than three years for a vaccine given to babies, the recommendation should be rejected. If less than two years for a toddlers and children, the recommendation should be rejected. If less than one year for adults, the recommendation should be rejected.

   b. Was the **sample size** sufficient to determine that the risks outweigh the potential benefits? Was the **sample population** representative and did the trial have appropriate subgroups based on race, comorbidities, etc.?

   c. What were the **adverse events**? What was the overall adverse event rate and what were the adverse event rates for specific harms?

   d. What was the **relative risk reduction**? What was the **absolute risk reduction**?

   e. Was the trial conducted **ethically**? Is there any evidence of corruption, financial conflicts of interest, or misreporting that might bias the results? Where was it conducted? Was it conducted at a contract research organization or academic institution? Has the manufacturer been convicted of any crimes and/or paid criminal penalties in the last ten years?

4. What is the **Number Needed to Vaccinate** to prevent a single case, hospitalization, ICU visit, and death?

5. How do the likely **benefits** of this intervention **compare** with the likely **harms** for each target population? Are the benefits observed actual health outcomes or inferred based on antibodies in the blood?