# NEJM Commentary: Funding for Post-Authorization Vaccine Safety Science

### What is the article about?

The *Perspectives* piece published in NEJM proposes a new way to fund post-authorization vaccine safety research in the U.S. The authors advocate amending a tax law to allow the surplus funds from the Vaccine Excise Tax to support the detection, investigation, and prevention of vaccine adverse reactions after a vaccine is approved for use.

### What has post-authorization vaccine safety looked like to date? How would this proposal improve current processes?

Before a vaccine is licensed for use, it must undergo phase I, II, and III prelicensure clinical trials where they are tested in thousands of participants. Throughout the trials, Data and Safety Monitoring Boards study and mitigate adverse reactions. Should a safety concern arise, trials are paused or discontinued. Following licensure, vaccine safety scientists continue to study the safety of vaccines as they are provided to larger populations than participated in the trials. Adverse events that happen after vaccination are most often unrelated and occur by chance. However, rare true reactions do occur and we do not always have a scientific explanation for them. Research about those reactions could enable us to explain them and possibly to prevent them These post-authorization studies inform guidance about who should receive a vaccine and how to prevent adverse reactions, such as contraindicating the vaccine in subgroups at high risk for serious adverse events.

We have seen many advancements in vaccine safety science since the Vaccine Injury Compensation Program was established. We have advanced knowledge of disease pathology and genomics, as well as opportunities to leverage big data through large healthcare databases. With adequate funding, we can further study even the rarest of adverse reactions to prevent them from occurring in the first place.

# Frequently Asked Questions

### 1. The National Childhood Vaccine Injury Act was passed in 1986. Why is an amendment necessary today? What has changed?

While the law was clearly intended to include science to prevent adverse reactions, at the time the science had not sufficiently evolved to do so. However, over the past 40 years our capacity to use large healthcare databases to determine or rule out possible associations between vaccines and adverse events following immunization and to determine the biological mechanism for adverse reactions has grown tremendously. We now have the capacity to rapidly conduct these studies with adequate resources. The time is now to amend the tax law to be consistent with the initial legislation, leading to major improvements in vaccine safety science to detect and reduce vaccine injuries, improve vaccine communication and confidence, and equitably compensate persons, who are injured by vaccines.

### 2. There has been a lot of concern about inadequate compensation for vaccine injuries (in general and for COVID19 vaccines), shouldn’t the trust fund surplus go to meet those needs instead?

COVID-19 compensation is through a separate program and not the vaccine injury compensation program (VICP). The VICP has run a substantial surplus every year.

### 3. Have you found congressional sponsors [or other supporters (e.g., government, industry, consumers) for your proposal?

We have not yet identified congressional or stakeholder support. This is an important next step.

### 4. Given how controversial and politically polarizing immunizations and vaccine safety have become in the US post-COVID, how do you expect your proposal to gain enough support to pass, especially in an election year?

Vaccines have historically received strong bipartisan support given their tremendous impact of saving lives and money. However, COVID has led to politicization around vaccines. Funding additional vaccine safety science affords the opportunity for political parties to come together on common ground and make an improvement important to Americans. Our approach is budget neutral – meaning that vaccine safety can be funded without impacting the deficit. This makes bipartisan support much more likely. Champions in Congress would be extremely helpful and serve as an opportunity for political leaders to show leadership by addressing a concern to Americans without costing the taxpayer more money.

### 5. All the adverse events of special interest (AESI) that you propose studying are rare, given the benefits of immunization vastly outweigh these rare risks, why should we invest in studying these rare risks?

Serious vaccine adverse reactions are rare. But when the vaccine is given to very large populations (as during the COVID19 pandemic for example), the total number affected is no longer negligible. It is important to find out which adverse events are causally related to vaccines, and which are coincidental. Careful studies of persons with vaccine-caused adverse reactions can lead to understanding the characteristics which are associated with the adverse reaction, and lead to development of more advanced vaccines or contraindicating the vaccine in those persons to prevent the occurrence of future adverse reactions.

Furthermore, when someone is vaccinated, they are usually not only trying to protect themselves, but they are also protecting their community, either voluntarily or under some kind of requirement. They reduce the chances that they will transmit the disease to someone who cannot be vaccinated (e.g., someone with a legitimate medical contraindication) or is too young to be vaccinated or was vaccinated and the vaccine didn’t work for them (no vaccine is 100% effective). Given vaccination protects society and the government has such an active role in developing, purchasing and promoting vaccines, society and the government has an obligation to compensate people truly injured by vaccines. Thus, even if risks are rare, those persons who are injured should be compensated. Research is needed to update this program.

Finally, preventing rare adverse reactions from vaccines will help improve public confidence in our vaccine program.

### 6. Given how rare these AESI’s are (e.g., one to three excess cases of Guillain-Barre Syndrome (GBS) per million influenza vaccine recipients in some seasons), how do you realistically expect to study them affordably?

With current rates of influenza vaccination, we would expect a few hundred cases of post-vaccination GBS per year in the US and more globally. Large healthcare databases now afford the opportunity to study even such rare adverse reactions.

### 7. Since the benefits of a safer vaccine extend outside of the US, shouldn’t the global community contribute their fair share?

It is important for vaccine safety efforts to be funded and conducted globally both to share the burden (costs) and take advantage of what can be learned in other and across countries. The Global Vaccine Data Network (GVDN) is doing these studies globally. The Institute for Vaccine Safety (IVS) and the National Institute of Health Foundation (FNIH) are forming a public-private partnership to leverage global resources.

### 8. Some vaccine companies (e.g., Moderna and Pfizer) made huge profits during the pandemic, why shouldn’t they (vs. taxpayer) fund making their vaccines safer?

Vaccine companies already spend a lot of resources to study their vaccines and make them safer when possible. However, there are needs beyond single vaccines and it is the responsibility of the government to make sure the public’s needs are fully met given the important role the government already plays in vaccines (funding vaccine research, recommending vaccines, purchasing vaccines, requiring vaccines for school entry, etc). The current excise tax on vaccines (75 cents per disease prevented) is already being collected. We propose the surplus from this tax be used to study vaccine safety and prevent adverse reactions. As this is budget neutral, it would not cost taxpayers more money.

### 9. If your proposal is successful, how would the funds be allocated?, Who would provide oversight over it? Would non-traditional researchers like Dr. Wakefield be eligible?

We recommend that the National Academy of Medicine conduct an independent and comprehensive review to address these important and complex issues of structure and governance. The highest quality research should be funded.

### 10. Should vaccine critics, such as RFK Jr be involved in determining how best to spend the money?

We recommend that the National Academy of Medicine conduct an independent and comprehensive review to address these important and complex issues of structure and governance.

### 11. Please explain the difference between the NCVIA and the tax code that funded it and what part are you propose amending.

The [NCVIA (PHL 99-660)](https://www.hrsa.gov/sites/default/files/hrsa/vicp/title-xxi-phs-vaccines-1517.pdf) created the vaccine injury compensation program, provided liability protection to vaccine manufacturers and healthcare providers, required healthcare providers to keep vaccine records, required CDC and FDA to create VAERS, required HHS to provide Congress annual vaccine safety reports, and created the National Vaccine Advisory Committee. Section 2127 of [NCVIA](https://www.hrsa.gov/sites/default/files/hrsa/vicp/title-xxi-phs-vaccines-1517.pdf) (p. 1336) is titled “Mandate For Safer Childhood Vaccines” and calls for:

“In the administration of this subtitle and other pertinent laws under the jurisdiction of the Secretary, the Secretary shall:

(1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on the effective date of this part 27 and promote the refinement of such vaccines, and

(2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.”

The clear intent of the law was to study vaccine safety and prevent adverse reactions.

Unfortunately, the tax code (26 U.S. Code § 9510) created the funding for NCVIA restricted use of the funds only for compensation and running the compensation program. We are recommending this tax code be amended to use the funds for the full intent of NCVIA.

### 12. What will guarantee that enhancements to the present system will really improve vaccine safety monitoring?

There are tremendous opportunities in big data through large healthcare databases and advanced knowledge of disease pathology and genomics that can be realized with adequate funding. The science is ready.

### 13. What should be done with this additional funding? What science is needed?

There are a broad range of vaccine safety activities that would greatly benefit from additional funding:

* Domestic passive and active surveillance
* Standard case definitions
* Clinical Immunization Safety Assessment (CISA) services rolled out nationally
* Vaccine safety biobank
* Genomic and other -omic studies for pathogenesis studies
* Global active surveillance
* Investigator initiated research
* Academic Centers of Excellence
* Public and stakeholder engagement
* Special studies of emergent issues
* Communications
* Administrative technical expertise, management, oversight
* Advisory committee
* Training program

### 14. How do ongoing post-authorization vaccine safety studies impact current vaccination campaigns?

While we want to continue to study possible adverse events to determine if they are caused by the vaccine and to further reduce the incidence of such adverse events, which remain rare, we know that the benefits of vaccines still far outweigh the risks for the vast majority of people. Vaccinations should continue according to the CDC’s immunization schedule.

### 15. In addition to lack of resources, why has vaccine safety research been so challenging?

With any medicine (including vaccines), we are interested in its safety and efficacy. But safety, unlike efficacy or effectiveness, generally cannot be measured directly. It can only be inferred indirectly from the absence of multiple possible adverse events following immunizations (AEFI), given the number of persons vaccinated. But if there is not a standardized case definition available for the AEFI, and a monitoring system is not in place, then a case of AEFI can be easily missed, especially if it’s rare. Even if both a case definition and monitoring are in place, if not enough persons who received the vaccine are monitored, then the AEFI can still be missed. This is the case when the sample size of the pre-authorization trials of a new vaccine is too small (e.g., ~10,000 persons) to detect a rarer risk.

Adequate funding of post-authorization monitoring of vaccine safety, once the vaccine is used in larger populations is therefore critical. The US uses [multiple complementary data systems](https://www.cdc.gov/vaccinesafety/index.html), each with their respective strengths and weaknesses to do so. It is also critical to assess whether clinical illnesses that occur after vaccination are causally or coincidentally related to vaccination. When millions of persons are vaccinated, there will be some who come down with serious illnesses purely by coincidence since unfortunately, bad illnesses occur every day in the world. Having a system to evaluate whether adverse events are causal or coincidental it critical to optimizing vaccination policy so the benefits are much greater than any harms.

## Additional References

### Legislation

* 1. [NCVIA (PHL 99-660)](https://www.hrsa.gov/sites/default/files/hrsa/vicp/title-xxi-phs-vaccines-1517.pdf)
	2. [26 U.S. Code § 9510](https://www.govregs.com/uscode/title26_subtitleI_chapter98_subchapterA_section9510)

### Vaccine Safety Papers

2.1 Salmon DA, Chen RT, Black S, Sharfstein J. Lessons learned from COVID-19, H1N1, and routine vaccine pharmacovigilance in the United States: a path to a more robust vaccine safety program. Expert Opin Drug Saf. 2024 Feb;23(2):161-175. doi: 10.1080/14740338.2024.2305707. Epub 2024 Feb 11. PMID: 38343204.

2.2 Lainie Rutkow, Brad Maggy, Joanna Zablotsky & Thomas R. Oliver, [Balancing Consumer and Industry Interests in Public Health: The National Vaccine Injury Compensation Program and Its Influence During the Last Two Decades](https://ideas.dickinsonlaw.psu.edu/dlra/vol111/iss3/5), 2007;111 DICK. L. REV. 681.

2.3 Faksova K, Walsh D, Jiang Y, et al. [COVID-19 vaccines and adverse events of special interest: A multinational Global Vaccine Data Network (GVDN) cohort study of 99 million vaccinated individuals](https://pubmed.ncbi.nlm.nih.gov/38350768/). Vaccine. 2024 Apr 2;42(9):2200-2211. doi: 10.1016/j.vaccine.2024.01.100. Epub 2024 Feb 12. PMID: 38350768.

2.4 Chen RT. [Vaccine risks: real, perceived and unknown](https://pubmed.ncbi.nlm.nih.gov/10559533/). Vaccine. 1999 Oct 29;17 Suppl 3:S41-6. doi: 10.1016/s0264-410x(99)00292-3. PMID: 10559533.

### Websites

3.1. [The Institute for Vaccine Safety (IVS), Johns Hopkins University School of Public Health](http://vaccinesafety.edu/)

3.2. [The Brighton Collaboration, a program of the Task Force for Global Health](https://brightoncollaboration.org/)

3.3. [National Academy of Medicine. Vaccine Safety Reports (as compiled by IVS)](https://www.vaccinesafety.edu/vaccine-safety-reports/)

3.4. [Global Vaccine Data Network (GVDN)](https://www.globalvaccinedatanetwork.org/)

3.5. [International Network of Special Immunization Services (INSIS)](https://insisvaccine.org/)