
Vaccine Safety Quarterly

Brighton Collaboration 2.0

Frederick Varricchio, PhD, MD - *Editor in Chief* Les Garber - *Style Editor*

Winter 2020

Dear Brightonians,

Welcome! This marks the first issue of the Vaccine Safety Quarterly (VSQ) after last year's transition of the Brighton Collaboration (BC) Secretariat from Basel, Switzerland to the Task Force for Global Health in Decatur (next to Atlanta), Georgia. If you missed the update providing the background for this change from BC 1.0 to 2.0, you can read it [here](#).

Due to strict Swiss privacy laws, we unfortunately were unable to transfer the BC 1.0 membership information and had to ask you to re-enroll in BC 2.0. If you didn't get this request, you can still do so [here](#) to make sure you maintain your active relationship with the Brighton Collaboration to help build trust in the safety of vaccines through rigorous science. After you enroll, you will receive a survey to tell us a little about yourself and where you would like the Brighton Collaboration to head. Stay tuned to future VSQ issue for the results.

As you can imagine, this has been a very busy period. The BC Secretariat and Science Board will use the VSQ to inform you about new developments in BC 2.0 and vaccine safety more generally. I'm excited therefore that Dr. Fred Varricchio has agreed to take on the role of editor of the VSQ. We worked jointly for a decade on the US Vaccine Adverse Event Reporting System (VAERS). Fred shares more of his thoughts below on how he plans to make VSQ an interesting and worthwhile short read for you.

Much of my time in 2019 was devoted to launching the [Safety Platform for Emergency Vaccines \(SPEAC\)](#) project funded by the [Coalition for Epidemic Preparedness and Innovation \(CEPI\)](#).

Several former and current BC Science Board members (Steve Black, Barbara Law, Wan-Ting Huang, Miriam Sturkenboom, Sonali Kochhar) are also involved. As SPEAC and BC 2.0 expand its activities, we look forward to soliciting your engagement and advice to meet the increasing needs for rigorous science in vaccine safety. Fred and I also look forward to you sharing information in the VSQ about your work and organization with other Brightonians. Vaccine safety works predominantly with rare/orphan outcomes, so cross sourcing our collective wisdom is much needed.

In closing, let me thank again the BC 1.0 team (Jan Bonhoeffer, Uli Heininger, Jorgen Bauwens, Simone Casagrande, David Nalin) for nurturing Brighton Collaboration into the "brand" it has become. I also want to thank the new BC 2.0 team (Matt Dudley, Jim Mootrey, Lisa Chung) as we build and improve on this legacy.



Robert (Bob) T. Chen

Scientific Director
Brighton Collaboration

New Editors

Frederick Varricchio, PhD, MD, Editor in Chief

Fred Varricchio spent thirteen years at the US Food and Drug Administration (FDA) mostly evaluating VAERS reports. He has approximately ninety publications from biochemistry and Molecular Biology to adverse event case definitions. He has been involved with BC working groups continuously since 2000. Previous jobs were at the University of Freiburg, Germany, the French National Research Center in Marseille, France, Yale Medical School and Memorial Sloan Kettering Cancer Center. Fred was also a Flight Surgeon in the US Air Force Reserve for fourteen years.

Les Garber, MEd, Style Editor

Les has been involved in elementary and secondary education throughout his entire career. Working with international, indigenous and American teachers and students has made 40+ wonderful years experience. Les is glad to volunteer some of his past printing and newsletter skills to the VSQ.

Note to the Reader

With this issue, we are resuming the VSQ with some personnel changes. The new editors responsible for VSQ are listed below. A current list of staff and addresses is on the last page of this VSQ, and the VSQ.

A survey was completed recently to determine the Brighton Collaboration's future interests and needs. Results will be shared in a future VSQ and implemented as possible.

We invite your comments and communications sent to any one of us. Especially, pass on any projects started, new results, or your thoughts on what needs doing. The VSQ is your place to network with your vaccine safety colleagues.

The U.S. National Vaccine Injury Compensation Program (VICP)

Dr Fred Varricchio

We propose publishing information on various vaccine safety infrastructure programs in different countries - learning from our similarities and differences. Please submit an article about how this (or other) vaccine safety issue is handled in your country.

The [US VICP](#) was established in 1988. There are two objectives: 1) to ensure a stable vaccine supply by limiting liability for vaccine manufacturers and vaccine administrators and 2) to ensure that individuals injured by certain vaccines are provided with fair and efficient compensation. This provides an alternative to civil litigation. It is a no-fault program with simplified requirements. Claims are initially evaluated by VICP physicians with consultants

as needed. Qualifying claims are submitted to a special master for final decisions.

[A table of included vaccines and corresponding injuries with chronological restrictions has been developed.](#) The program is funded by a \$0.75 tax per dose of covered vaccine. To date about 21,000 claims have been filed and 7,000 compensated.

[Success of the program is indicated by vaccine market stabilization with reduced supply shortages, new vaccines being introduced and price stabilization.](#)

[Halabi and Omer have proposed a Global Vaccine Injury Compensation Program.](#)

Abstracts

Numerous articles on vaccine safety have appeared since the last VSQ. We have selected four to present here that you might otherwise miss. Would anyone like to organize a Journal Club on any of these or other topics?

Drs. Fred Varricchio and Matthew Dudley

1. Article Of Interest Because It Discusses Vaccine Efficacy In Immunocompromised Recipients This could relate to arguments about overloading the immune system with vaccines.

Title: [Safety and efficacy of inactivated varicella zoster virus vaccine in immunocompromised patients with malignancies: a two-arm, randomized, double-blind, phase 3 trial](#)

Lancet Infect Dis. 2019 Sep;19(9):1001-1012. doi: 10.1016/S1473-3099(19)30310-X

Corresponding Author: Dr Kathleen M Mullane (Department of Medicine, University of Chicago, Chicago IL USA)

Introduction: “Patients who are immunocompromised because of malignancy have an increased risk of herpes zoster and herpes zoster-related complications. We aimed to investigate the efficacy and safety of an inactivated varicella zoster virus (VZV) vaccine for herpes zoster prevention in patients with solid tumor or hematological malignancies.”

Main Findings: “The inactivated VZV vaccine was well tolerated and efficacious for herpes zoster prevention in patients with solid tumor malignancies receiving chemotherapy, but was not efficacious for herpes zoster prevention in patients with hematological malignancies.”

2. This May Be Relevant To The Newly Described Acute Flaccid Paralysis Of Unknown Cause But An Enterovirus Has Been Suggested As A Cause.

Title: [Immunogenicity and safety of an inactivated enterovirus A71 vaccine in children 3–6 years and 2–35 months of age- an open-label, randomized phase IIb clinical trial](#)

Vaccine. 2019 Sep 3;37(37):5559-5566. doi: 10.1016/j.vaccine.2019.07.096.

Corresponding Author: Miao-Chiu Hung (Division of Infectious Diseases, Department of Pediatrics, Taipei Veterans General Hospital, Taiwan, ROC)

Introduction: “Enterovirus A71 (EV-A71) infection can cause severe debilitating complications and even death in young children. The immunogenicity and safety of an inactivated whole EV-A71 virus vaccine were assessed in children 2 months to 6 years of age.”

Main Findings: “This EV-A71 vaccine containing adjuvant is immunogenic and safe in children 2 months to 6 years of age.”

3. Discusses How Opinions May Change At The Actual Moment Requiring A Decision

Title: [Vaccine-Hesitant and Vaccine-Refusing Parents' Reflections on the Way Parenthood Changed Their Attitudes to Vaccination](#)

J Community Health. 2019 Aug 7. doi: 10.1007/s10900-019-00723-9

Corresponding Author: T. Rozbroj (Australian Research Centre in Sex, Health and Society, La Trobe University, Bundoora VIC Australia)

Introduction: "Having children compels parents to examine their vaccine beliefs, particularly if they are vaccine-hesitant or refuse all vaccines. Presently, little is known about the specific ways in which having children influences the vaccine beliefs of parents. This research examined how having children changed the attitudes of Australian vaccine-hesitant and vaccine-refusing parents towards childhood vaccination."

Main Findings: "Hesitant and refusing parents' interpreted vaccine choices through a lens of distrust of pharmaceutical companies and regulatory bodies overseeing vaccine safety. The distrust fueled parents' fears about vaccination risks, such as side effects. Parents became concerned about the scheduled timing of vaccinations, particularly of the Hepatitis B vaccine."

4. Interesting Because It Provides an Overview of One Manufacturer's Activities In Adverse Event Surveillance.

Title: [Varicella Virus Vaccine Live: A 22-Year Review of Postmarketing Safety Data](#)

Open Forum Infect Dis. 2019 Aug 1;6(8). pii: ofz295. doi: 10.1093/ofid/ofz295.

Corresponding Author: Meredith Woodward (Merck & Co., Inc., Kenilworth NJ USA)

Introduction: "Varicella, a contagious infectious disease caused by varicella zoster virus (VZV), can result in hospitalization and, occasionally, death. Varicella virus vaccine live (VVVL [VARIVAX]) was introduced in the United States in 1995. This comprehensive review of the VVVL safety profile is based on 22 years of postmarketing adverse event (AE) data received through spontaneous and non-interventional study reports submitted by health care providers and on a review of the published literature (cumulatively from March 17, 1995, through March 16, 2017, during which period >212 million doses were distributed globally)."

Main Findings: "The VVVL safety profile was consistent with previous publications, with common AEs including varicella, rash, and pyrexia. AE reports have decreased over time, from ~500 per million doses in 1995 to ~40 per million doses in 2016; serious AEs comprise 0.8 reports per million doses. Secondary transmission was rare (8 confirmed cases); polymerase chain reaction analysis indicated that 38 of the 66 reported potential secondary transmission cases of varicella were attributable to wild-type VZV. The prevalence of major birth defects in the Pregnancy Registry was similar to that in the general US population. In total, 86 cases of death were reported after vaccination with VVVL; immune-compromised individuals appeared to be most at risk for a fatal varicella- or herpes zoster-related outcome. This comprehensive 22-year review confirms the overall safety profile for VVVL, with no new safety concerns identified."

World Health Organization (WHO) Global Vaccine Safety Summit Report

Drs. Matthew Dudley and Robert Chen

[The Global Vaccine Safety Summit](#), organized by the World Health Organization, took place December 2-3 2019 in Geneva, Switzerland. During the Summit, the current draft of the Global Vaccine Safety Blueprint 2.0 (GVS2.0) was presented on Day 1 and input for the final version was collected, [including those from Dr. Chen](#).

The first Global Vaccine Safety Blueprint (GVS1.0) was published in 2012 and described the goals of vaccine safety systems in two parts: minimal capacity and enhanced capacity. GVS2.0 will expand on this by incorporating the non-dichotomous concept of maturity level. GVS2.0 will also build upon GVS1.0 by focusing on the following areas to maximize impact in the next decade regulatory framework: AEFI surveillance, enhanced vaccine safety communication, coordination of safety systems, and fragile states and crisis situations.

On Day 2, the 20th anniversary of the WHO's Global Advisory Committee on Vaccine Safety (GACVS) was celebrated with a symposium based on four situation papers:

- Safety issues from the early years that have been scientifically clarified but can still

affect vaccine confidence and acceptance (auto-immunity, thimerosal, aluminium adjuvants, autism, immune overload, non-specific effects)

- Novel safety issues and areas that require further research (e.g. narcolepsy, dengue vaccines, intussusception, HPV vaccine, RTS)
- Novel vaccines and vaccine products (viral vectors, novel adjuvants, highly multivalent vaccines, DNA vaccines, thermostable vaccines, monoclonal antibodies, micro patch...); Dr. Chen is one of the co-authors.
- Methodological frontiers (qualifying available evidence for rare events, use of distributed data network to monitor vaccine safety issues, monitoring the safety of pregnancy interventions, capacity building and Blueprint 2.0)

After the conclusion of the Summit, Brighton Collaboration members gathered for an informal dinner at an Indian restaurant in downtown Geneva. The food and drinks were both delicious and plentiful. The company was excellent; and a good time was enjoyed by all. If you missed it, never fear, as more such gatherings will be organized in the future.

Lasker-Bloomberg Public Service Award

The 2019 Lasker award has been awarded to Global Alliance for Vaccine and Immunization (GAVI). GAVI was formed after the 2000 Davos World Economic Forum to increase access to new and underused vaccines. Using new approaches to obtain and deliver vaccines in low-income countries, 750 million children have been vaccinated and the cost of a full course of WHO recommended vaccines reduced

to US \$27. GAVI has functioned in over 50 countries and as a result of GAVI's initial help 15 countries have left the program and are able to continue an immunization program on their own. Gavi continues to innovate by developing new vaccines, Ebola, and delivery methods, drones. It is estimated that US \$ 1 invested in vaccines in a GAVI supported country averts US

\$ 21 in the cost of illness (JAMA. 322, 1051, 2019)

The struggle goes on...

These are three items which appeared in local newspapers recently.

[Cartoon](#) (Venice Gondolier, October 2019; Cable Cartoons)

[Strict Vaccine Law Tumbles in New Jersey Legislature](#) (New York Times, December 2019)

[Dr. John Robbins, Developer of a Meningitis Vaccine, Dies at 86](#) (New York Times, December 2019)



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