Polio Vaccine Safety
Paul Meier's Role in the Discovery and Evaluation of The Cutter Incident

Professor Chris Barker, Ph.D.
Adjunct Associate Professor of Biostatistics, UIC SPH.

www.barkerstats.com

Contents

Background

In 2020, during the covid19 pandemic, several pharmaceutical companies are conducting Phase III randomized blinded clinical trials for a vaccine to give immunity to the virus, SARS-COV-2 that causes the disease covid19. Phase III Clinical trial protocols are available online for download for Moderna, AstraZeneca/Oxford and Pfizer /BioNtech. Johnson & Johnson has started enrolling a phase III clinical trial. Vaccines manufactured in China and Russia possibly skipped a Phase III step and administered a vaccine directly to health care workers- The details about Russian And Chinese vaccines are sketchy and difficult to confirm- these vaccines are not available in the US.

Astra Zeneca/Oxford recently suspended a clinical trial for safety . Dr. Fauci at NIAID has stated (paraphrasing) that this is evidence the "process works safety evaluation of vaccine". Several of my friends and colleagues recalled "problems with the polio vaccine". I recall, as I'm sure many of the readers, decades ago, visiting elementary school with my parents to get a sugar cube with a polio vaccine. And since that time, I have the vaguest memories of the fear of possibly getting polio and then being treated in an "iron lung".

I dug into the history in depth. During the Polio field trials, an event, forever known as "The Cutter Incident" was uncovered, somewhat dramatically, by Paul Meier during attendance at a seminar by Cutter scientists. This led to changes in evaluation of the safety of vaccines. I defer to others for the history of changes in vaccine review and legislation arising from the Cutter Incident.

Brief Polio Vaccine Overview

The safety concerns described in this note and the role of Paul Meier arose from the inactivated (Salk) vaccine IPV. Prior to the Salk and Sabin vaccines, two other vaccines, named after their developers, Kolmer and Brodle were withdrawn from use. Brodie was a "killed" virus and Kolmer was an attenuated virus (Halpern,2006) .
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472109/

There were two polio vaccines, one by Jonas Salk and the other by Albert Bruce Sabin. Salk announced his vaccine in 1953. Salk used "inactivated Polio virus" (IPV) and Sabin used "attenuated virus" also known as "oral polio vaccine" (OPV). Salk deactivated virus using Formalin (formaldehyde) . Salk also collaborated with Pfizer for the large-scale manufacturing of the vaccine. An interesting historical note that the Sabin vaccine was tested and proven safe in tests 1957 in about 10.000,000 people in Russia (the former Soviet Union).
https://www.virology.ws/2015/09/10/why-do-we-still-use-sabin-poliovirus-vaccine/

I'll mention what seems to be possible second name for the Polio vaccine clinical trials. One author (Monto) refers to the trials as the Francis Field trials, named after Dr. Thomas Francis Jr. M.D. the overall director of the trials. Dr. Salk worked in Dr. Francis' department of Epidemiology at Johns Hopkins. Dr. Monto also makes a remarkable comment about "slavish reverence to significance testing" and the absence of p-values in the final report of vaccine results, excerpted at length here

The essential results are shown in table 2, with little modification from the way they were originally presented except for certain combination of groups. An unusual feature in the table, to the modern reader, is the lack of any reference to statistical significance. This did not indicate, as will be discussed, that statistical issues, especially *p* values, were not recorded as a necessary consideration, but, rather, it reflected the era and the lack of our current slavish reverence for significance testing often over other relevant concerns. It also may have indicated the realization that differences in this trial could have been statistically significant even in the absence of effects that would have been important from a public health standpoint, given its large size.
Source: Monto

I (re-)discovered an event, forever after called the "Cutter Incident". I (re-) discovered that Paul Meier was part of a team in 1955 that discovered that Cutter Laboratories had not correctly attenuated the live polio virus. Worse, it appears that Cutter had been hiding details of the "virus attenuation". Children receiving the vaccine developed a polio like illness later described as the "largest biological disaster in the History of the US". Laws and safety review of vaccines changed because of the cutter incident. Below I cite some of the legal outcomes and defer to others for the complete history of the litigation following cutter.

Polio Vaccine Manufacturing Data Suppression

The nearly unfathomable discovery of Cutter was the discovery data suppression. Excerpting at length from Paul's paper,

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3477951/

Excerpting from Betts 2012.

"But the biggest issue, for Meier, emerged during a seminar attended by many of the researchers working on the project, where it became apparent that members of the team were suppressing the data related to some of the test vaccine lots. As soon became clear,

the polio virus used in the trial vaccines was not always properly inactivated. Jonas Salk, the vaccine's inventor, "cut out data in order not to show what happened to some lots," Meier charged. He said that the National Foundation for Infantile Paralysis, which sponsored the study, dropped from its advisory committee scientists who did not agree with how the results were being presented.

The field trial's findings were reported to show the vaccine's effectiveness, over the objections of some of the committee members, Meier said. Soon after, the US Public Health Service reported cases of paralytic polio in children inoculated with the vaccine. The original cases were traced back to lots produced by Cutter Laboratories, of Berkeley, CA, one of six manufacturers licensed to produce the vaccine. However, Meier said that the problem was more widespread. He said:

I got some data from a physician who was working on this, and we found that not only was Cutter wrong, but there were various other companies that had the same polio virus in their samples, although not as much as the samples from Cutter Laboratories. But because there were so many improperly diagnosed cases out there, and because the other manufacturers went around to various newspapers and threatened to cut their advertising, it was dumped on Cutter. Cutter was responsible because they did things in producing and testing the vaccine they were told not to do".

Biological Disaster? How Serious was the vaccine manufacturing problem?

Children developed a polio like illness Vaccine-associated paralytic poliomyelitis (VAPP)

https://www.cdc.gov/vaccinesafety/concerns/concerns-history.html

Excerpting from the CDC

...In April 1955 more than 200 000 children in five Western and mid-Western USA states received a polio vaccine in which the process of inactivating the live virus proved to be defective. Within days there were reports of paralysis and within a month the first mass vaccination programme against polio had to be abandoned. Subsequent investigations revealed that the vaccine, manufactured by the California-based family firm of Cutter Laboratories, had caused 40 000 cases of polio, leaving 200 children with varying degrees of paralysis and killing 10....

and excerpting about the law, from Fitzpatrick review of the book by Offitt.

Near Elimination of Vaccine development by lawsuits

Vaccine Safety evaluation, manufacturing and the law changed because of the Cutter Incident. Excerpting from Offit.
...The Cutter incident had an ambivalent legacy. On the one hand, it led to the effective federal regulation of vaccines, which today enjoy a record of safety `unmatched by any other medical product'. On the other hand, the court ruling that Cutter was liable to pay compensation to those damaged by its polio vaccine—even though it was not found to be negligent in its production—opened the floodgates to a wave of litigation. As a result, `vaccines were among the first medical products almost eliminated by lawsuits'. Indeed, the National Vaccine Injury Compensation Program was introduced in 1986 to protect vaccine manufacturers from litigation on a scale that threatened the continuing production of vaccines. Still, many companies have opted out of this low-profit, high-risk field, leaving only a handful of firms to meet a growing demand (resulting in recent shortages of flu and other vaccines)....

CDC lists safety concerns for other approved vaccines
https://www.cdc.gov/vaccinesafety/concerns/concerns-history.html

Meier's evaluation of the safety recommendations following The Cutter Incident

I commend readers of this note to obtain a copy of Pauls' article in Science 1957. (I have a copy if this proves to be insurmountable problem – I can't post due to copyright issues). Paul reviewed recommendations for the detection of live virus in the "vaccine lots". Paul considers issues ranging from first order kinetics in virology to the societal public health implications. Paul's review I can only describe as a deeply thoughtful, calm assessment and re-assessment of manufacturing and vaccine safety evaluation.

Excerpting Paul's concluding remarks and advice from his 1957 paper, advice that remains valid today

From the viewpoint of the relationships between scientists and the general public, the consequences of this policy may be much more serious than the harm done by faulty vaccine. It is understandable that, having decided to proceed with a program, all concerned should wish to have it presented in the most favorable light. However, failure adequately to inform the public, more particularly the physicians who must largely accept the responsibility for advising the rest of the public, seems likely to lead to the

deterioration of the confidence and respect which scientists should enjoy. In view of the questions raised about the general policies adopted in the safety-testing program for poliomyelitis vaccine, a searching study of the entire program conducted by an appropriate body, such as the National Academy of Sciences, seems called for. Such a study could lead to recommendations for future programs which would provide for more complete access to information and, consequently, to more adequate protection from errors in judgment.

Polio Vaccine Side effects

The polio vaccine side effect arising from lots with active virus is called Vaccine-associated paralytic poliomyelitis (VAPP)

https://www.cdc.gov/vaccinesafety/concerns/concerns-history.html

CDC historical concerns with Polio Vaccines

In 1955, some batches of polio vaccine given to the public contained live polio virus, even though they had passed required safety testing. Over 250 cases of polio were attributed to vaccines produced by one company: Cutter Laboratories. This case, which came to be known as the Cutter Incident, resulted in many cases of paralysis. The vaccine was recalled as soon as cases of polio were detected.

The Cutter Incident was a defining moment in the history of vaccine manufacturing and government oversight of vaccines and led to the creation of a better system of regulating vaccines. After the government improved this process and increased oversight, polio vaccinations resumed in the fall of 1955.

At the time, there was no system in place to compensate people who might have been harmed by a vaccine. Today we have the National Vaccine Injury Compensation Programexternal icon (VICP), which uses scientific evidence to determine whether a vaccine might be the cause of an illness or injury, and provides compensation to individuals found to have been harmed by a vaccine. The VICP remains a model method for ensuring that all persons harmed by vaccines are compensated quickly and fairly, while also protecting companies that make lifesaving products from financially unsustainable liability claims through the tort system.

For more information, see Food and Drug Administration (FDA)'s Science and the Regulation of Biological Productsexternal icon page.

Legislation resulting from Cutter

At the time, there was no system in place to compensate people who might have been harmed by a vaccine. Today we have the National Vaccine Injury Compensation Programexternal icon (VICP), which uses scientific evidence to determine whether a vaccine might be the cause of an illness or injury, and provides compensation to individuals found to have been harmed by a vaccine. The

VICP remains a model method for ensuring that all persons harmed by vaccines are compensated quickly and fairly, while also protecting companies that make lifesaving products from financially unsustainable liability claims through the tort system.

Conclusion

A fundamental principle of vaccine for a lethal illness is the trust by the population of people at risk in the adequacy of the evaluation of efficacy and safety and the honesty and integrity of the scientists involved. The Cutter Incident is considered to be the largest biological disaster in the history of the US or vaccine development. Paul Meier was a central figure in the discovery, methodical reporting and interpretation of the findings of the investigation. Paul identified "root causes". Remarkably, Pauls' published interview comments (Marks) seems to suggest that Paul believes his 1957 paper in Science may have been ignored.

Paul certainly collaborated with many others in the discovery of the Cutter Incident. Paul left no stone unturned in his 1957 assessment in Science. In 2020, about 63 years later, in the middle of an unprecedented pandemic by covid19, Pauls' evaluation of Cutter manufacturing and his publication is a pillar in the process of establishing vaccine safety.

References

Betts, Kellyn. "Paul Meier A Man Behind the Method." *American journal of public health* 102.11 (2012): 2026-2029.

Brownlee, K. Alexander. "Statistics of the 1954 polio vaccine trials." *Journal of the American Statistical Association* 50.272 (1955): 1005-1013.

Dublin, Thomas D. "1954 Poliomyelitis Vaccine Field Trial: Plan, Field Operations, and Follow-up Observations." *Journal of the American Medical Association* 158.14 (1955): 1258-1265.

Fitzpatrick, Michael. "The cutter incident: How america's first polio vaccine led to a growing vaccine crisis." *Journal of the Royal Society of Medicine* 99.3 (2006): 156-156.

Halpern, Sydney A. *Lesser harms: The morality of risk in medical research*. University of Chicago Press, 2006.

Hinman, Alan R., and Stephen B. Thacker. "Invited Commentary on "The Cutter Incident: Poliomyelitis following Formaldehyde-inactivated Poliovirus Vaccination in the United States during the Spring of 1955. II. Relationship of Poliomyelitis to Cutter Vaccine"." *American Journal of Epidemiology* 142.2 (1995): 107-108.

Marks, Harry M. "A conversation with Paul Meier." *Clinical Trials* 1.1 (2004): 131-138.

Marks, Harry M. "The 1954 Salk poliomyelitis vaccine field trial." *Clinical Trials* 8.2 (2011): 224-234.

Meier, Paul. "TIIE BIGGEST PUBLIC IIEALTH EXPERIMENT EVER: The 1954 Field Trial of the Salk Poliomyelitis Vaccine."

Monto, Arnold S. "Francis field trial of inactivated poliomyelitis vaccine: background and lessons for today." *Epidemiologic reviews* 21.1 (1999): 7-23.

Nathanson, Neal, and Alexander D. Langmuir. "The Cutter Incident. Poliomyelitis following Formaldehyde-Inactivated Poliovirus Vaccination in the United States during the Spring of 1955. II. Relationship of Poliomyelitis to Cutter Vaccine." *American journal of hygiene* 78.1 (1963): 29-60.

Offit, Paul A. The Cutter incident: how America's first polio vaccine led to the growing vaccine crisis. Yale University Press, 2007.

U.S. Public Health Service, Technical Report on Salk Poliomyelitis Vaccine (mimeographed)
(June 1955).

Reference URLs

Washington Post, April 4, 2020,
https://www.washingtonpost.com/history/2020/04/14/cutter-polio-vaccine-paralyzed-children-coronavirus/

History.com

https://www.history.com/this-day-in-history/salk-announces-polio-vaccine

Science history.com

https://www.sciencehistory.org/historical-profile/jonas-salk-and-albert-bruce-sabin