UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
AND THE FOOD AND DRUG ADMINISTRATION

PETITION FOR ADMINISTRATIVE ACTION TO REQUIRE CLINICAL TRIAL OF IPOL TO ASSESS THE SAFETY OF THIS PRODUCT	**:**	**Docket No.**

CITIZEN PETITION

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CITIZEN PETITION

This petition is being submitted pursuant to 21 C.F.R. § 10.30 and related relevant provisions of the Federal Food, Drug, and Cosmetic Act and Public Health Service Act, the Public Health and Welfare at, *inter alia*, 42 U.S.C. § 262(a)(2)(A)-(C), 42 U.S.C. § 262(j), and 42 U.S.C. § 300aa-10 *et seq.*, to request that the Commissioner of Food and Drugs (the "**Commissioner**") withdraw or suspend the approval granted by the Food and Drug Administration ("**FDA**") for IPOL for infants and toddlers until a properly controlled and properly powered double-blind trial of sufficient duration is conducted to assess the safety of this product as required pursuant to applicable federal statutes and regulations for licensing this product. *See, e.g.*, 21 U.S.C. § 393 (The FDA "shall promote the public health by … reviewing clinical research and taking appropriate action … [to] protect the public health by ensuring that …. drugs are safe and effective.")

The clinical trials relied upon to license this product did not include a control group and only assessed safety for up to three days after injection. These trials therefore did not comply with the applicable federal statutory and regulatory requirements necessary to prove the product was "safe" prior to licensure. The FDA therefore must either withdraw or suspend the approval of this product until an appropriate clinical trial, as required by law, is conducted to determine its safety.

Furthermore, the product label for IPOL should be amended to note that this product does not prevent infection and transmission.

A. ACTION REQUESTED

1. Petitioner requests that the FDA withdraw or suspend the approval for IPOL for infants, toddlers, and children until a properly controlled and properly powered double-blind trial of sufficient duration is conducted to assess the safety of this product.

2. Petitioner further requests that the FDA amend the product label for IPOL to note that: "IPOL does not prevent intestinal infection and therefore does not prevent poliovirus transmission."

B. STATEMENT OF GROUNDS

3. IPOL is a vaccine for poliomyelitis. The Centers for Disease Control and Prevention ("**CDC**") Recommended Child and Adolescent Immunization Schedule recommends universal vaccination of all infants and children with inactivated polio vaccine ("**IPV**") with a 4-dose series administered at 2-months, 4-months, 6-months, and 4-years of age.[1] The only stand-alone vaccine for poliomyelitis used in the United States is Poliovirus Vaccine Inactivated

[1] *See* https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html#note-polio (last visited August 23, 2022).

(Monkey Kidney Cell), trade named IPOL, licensed in 1995 ("**IPOL**").[2]

4. IPOL is unlike the inactivated polio vaccine invented by Jonas Salk or the oral polio vaccine ("**OPV**"), made from a live attenuated virus, invented by Albert Sabin. As described in the package insert for IPOL, the "culture technique and improvements in purification, concentration, and standardization of poliovirus antigen produce a more potent and consistent immunogenic vaccine than the inactivated poliovirus vaccine (IPV) available in the US prior to 1988."[3] Indeed, while Salk's IPV contained 20, 2 and 4 D antigen units of PV types 1, 2, and 3, by introducing a new culture technique using cells on microcarrier beads in suspensions cultured in large stainless steel tanks, IPOL contains 40, 8 and 32 D antigen units of types 1, 2, and 3. Meaning, vaccine production methods for IPOL allow for higher concentrations of vaccine antigens in IPOL than were attainable in previous inactivated polio vaccines.[4]

5. Moreover, unlike Salk's vaccine, the virus used in IPOL is "grown in vero cells, a continuous line of monkey kidney cells cultivated on microcarriers."[5] Vero cells have modified chromosomes which cause them to multiple forever, like cancer cells.[6] These cells are susceptible to infection by dozens of viruses, including HPV, measles, rubella, reovirus, SV40 virus, and SV-5.[7]

6. The Informed Consent Action Network ("**ICAN**") is a non-profit organization that advocates for informed consent and disseminates information necessary for same with regard to all medical interventions. In 2017, a supporter of ICAN advised the organization that the clinical trial relied upon by the FDA to license IPOL reviewed safety for only three days after injection. ICAN found this claim incredible. It sounded nothing short of a conspiracy theory.

7. Indeed, the FDA states that the clinical trial relied upon for licensure is typically "1 to 4 years"[8] and that the duration of a clinical trial should "reflect the product and target condition."[9] The time frame for the safety review should be longer for minors, and in particular for babies and toddlers, since autoimmune, neurological, and developmental disorders will often not be diagnosed until after babies are at least a few years old.[10] Indeed, a 2019 review of 306

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[2] https://www.fda.gov/vaccines-blood-biologics/vaccines/ipol-poliovirus-vaccine-inactivated-monkey-kidney-cell (last visited August 23, 2022).

[3] https://www.fda.gov/media/75695/download (last visited August 23, 2022).

[4] *See McBean, A.M., A Comparison of the Serologic Response to Oral and Injectable Trivalent Polio Vaccine*, Rev Infect Dis., (May 1, 1984) available at https://www.icandecide.org/wp-content/uploads/2022/08/Combined-IPOL-production-Vol-1F-Vol.-4A-Vol.-4B.pdf.

[5] https://www.fda.gov/media/75695/download (last visited August 23, 2022)

[6] https://admin.phe-culturecollections.org.uk/media/122249/vero-cell-line-profile.pdf

[7] https://www.atcc.org/products/all/ccl-81.aspx#characteristics

[8] https://www.fda.gov/patients/drug-development-process/step-3-clinical-research (last visited August 23, 2022).

[9] https://www.fda.gov/media/102332/download (last visited August 23, 2022).

[10] For example, according to the CDC, even for a common neurological disorder such as ADHD, "5 years of age was the average age of diagnosis for children reported as having severe ADHD." https://www.cdc.gov/ncbddd/adhd/features/key-findings-adhd72013.html (last visited August 23, 2022). As another example, learning disabilities, a group of common developmental issues, are often "identified once a child is in school."

pediatric studies, authored by researchers at the FDA and Duke University, explained that, compared to licensing a drug for adults, "data on drug efficacy and safety in children may require an additional 6 years."[11]

8. Moreover, Congress mandated that the FDA only license drugs that their sponsors have proven to be "safe and effective." The FDA relies upon clinical trial reports provided by the sponsor of the drug to make this determination. The clinical trial information submitted must be sufficient to demonstrate the product is "safe." While there are many ways to demonstrate a product is safe, three days of safety data would be patently insufficient to demonstrate safety. Moreover, a trial lacking a proper control group renders any "safety" data of limited value.

9. Hence, the claim that IPOL was licensed by the FDA based on only a few days of safety data after each injection sounded like science fiction. ICAN simply found the claim not credible. That was until ICAN reviewed the package insert for IPOL which described its pre-licensure clinical trials. To ICAN's amazement, it indicates that safety in these clinical trials was reviewed for only three days after the injection of each dose into babies.

10. Hence, ICAN submitted a FOIA request to the FDA for, "A copy of the report for each clinical trial relied upon by the FDA when approving IPOL in 1990." The FDA subsequently provided four documents containing data from three pre-licensure clinical trials: (1) "A Comparison of the Serologic Response to Oral and Injectable Trivalent Polio Vaccine," by Dr. A. Marshall McBean and co-investigators (1984); (2) "Merieux Inactivated Poliovirus Vaccine Final Report of Clinical Studies at Suny/Children's Hospital, Buffalo, New York and Johns Hopkins University, Baltimore, Maryland," the final report on the study of P. Ogra and H. Faden (1989); (3) a progress report on the study of P. Ogra and H. Faden (1987); and (4) "Serologic Response to Oral Polio Vaccine and Enhanced-Potency Inactivated Polio Vaccines" (1988).

11. None of the studies relied upon by the FDA to license IPOL, either individually or collectively, prove the product was "safe" prior to licensure and, therefore, neither the product nor the FDA approval comply with the applicable federal statutory and regulatory requirements.

a. The first study by McBean did not address safety (it only addressed serologic response). This study cannot be used to support any finding of safety of IPOL.
b. The second document is a final study with two protocols in which IPOL was compared to a group received OPV or a combination of OPV and IPV. Many of the children also received the DTP vaccine concomitantly with the polio vaccine. In one protocol, the Buffalo protocol, the safety of IPOL was not reviewed after the actual immunization appointment. In the second protocol, the Johns Hopkins protocol, safety was reviewed via telephone call for only three days after each injection.
c. The third document is only an incomplete progress report of the above study.

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https://www.nichd.nih.gov/health/topics/learning/conditioninfo/diagnosed (last visited August 23, 2022). Even for asthma, a very common autoimmune condition, whose symptoms are obvious, diagnosis can be difficult for children under 5 years of age because lung function tests aren't accurate before 5 years of age and "[s]ometimes a diagnosis can't be made until later, after months or even years of observing symptoms." https://www.mayoclinic.org/diseases-conditions/childhood-asthma/diagnosis-treatment/drc-20351513 (last visited August 23, 2022).

[11] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6526087/.

d. The fourth document is a journal article reporting results of a trial wherein the serologic response to three doses of two enhanced potency IPVs was compared with the response to three doses of OPV. In that trial, children received either one of two IPV or OPV doses, in addition to the DTP vaccine. Parents were contacted three days after the vaccination of their children to report adverse reactions which occurred within 48 hours of administration

12. Clinical trials that only review safety for up to three days after administration, even assuming a proper control group, cannot support the safety of this product. As such, the FDA could not have fulfilled its statutory duty to assure the safety of IPOL prior to licensing it for injection into infants, toddlers, and children.

13. Furthermore, there is confusion in the marketplace as to the effectiveness of IPOL. It is widely, and wrongly, believed that this product can prevent infection and transmission. For example: *Polio in New York State - August 2022*, NY Department of Health, https://www.health.ny.gov/diseases/communicable/polio/ ("In communities with lower vaccination rates, polio can spread even more easily. … The best way to keep New York polio-free is to maintain high immunity across the population through vaccination.") (last visited Aug. 22, 2022); Mani, Neritan, MD, *Polio in New York in 2022: Are You at Risk?*, Health Matters (Aug. 19, 2022), https://healthmatters.wphospital.org/blog/august/2022/polio-in-new-york-in-2022-are-you-at-risk/ (According to the Associate Medical Director at White Plains Hospital, "Vaccination is strongly recommended to protect children and adults from the polio virus and to prevent it from spreading."); *Polio*, Cleveland Clinic, https://my.clevelandclinic.org/health/diseases/15655-polio (stating, "Vaccine-derived polioviruses can only spread where not many people are vaccinated.") (last visited Aug. 22, 2022).

14. But as the CDC recently explained, "IPV does not prevent intestinal infection and therefore does not prevent poliovirus transmission"[12] The FDA should therefore also amend the product label for IPOL to note that "IPOL does not prevent intestinal infection and therefore does not prevent poliovirus transmission."

15. The undersigned therefore respectfully urges that the action requested above be adopted forthwith.

C. ENVIRONMENTAL IMPACT

16. The undersigned hereby states that the relief requested in this petition will have no environmental impact and therefore an environmental assessment is not required under 21 C.F.R. Sections 25.30 and 25.31.

D. ECONOMIC IMPACT

17. Economic impact information will be submitted upon request of the commissioner.

[12] https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7133e2-H.pdf

E. CERTIFICATION

18. 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.

19. The Petitioner, therefore, respectfully urges that this request be granted forthwith.

Respectfully submitted,

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