

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



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RE: Docket Number 02N-0466

The American Academy of Pediatrics (AAP) and the 57,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical subspecialists we represent welcomes the opportunity to comment on the research protocol: **A Multi-Center, Randomized Dose Response Study of the Safety, Clinical and Immune Response of Dryvax® Administered to Children 2 to 5 Years of Age.** The Academy supports and believes that this study should be conducted.

Predicated on the level of risk of exposure known at this time to public health officials, the Academy, in its September 2002 "Smallpox Vaccine" policy statement (attached), asserts that the ring-vaccination strategy is the recommended avenue for dealing with a smallpox outbreak. However, as the proposed method of delivery (5 jabs) of the 1:5 dilution of the currently licensed smallpox vaccine has never been tested in children, the Academy recommends that the currently licensed vaccine needs to be tested under these circumstances. Additionally ongoing attempts to develop a safer and more effective smallpox vaccine should continue and should be supported. Smallpox vaccines, including those presently available and those developed in the future should be evaluated for safety and immunogenicity in children as well as adults."¹

The impetus to test smallpox vaccine in children arises from two separate risk scenarios. The first is the perceived or actual risk of a terrorist incident in which smallpox is disseminated in this country; the second risk for children is the possibility that, in the absence of a terrorist incident, the vaccine will be offered to the public on a voluntary or universal recommendation basis. The Academy believes it is unwise, and may be unethical, to offer a vaccine to children, either on an emergency or volunteer basis, that has not been tested in children.

In light of the risks outlined above, the Academy answers the questions specifically posed in the above named docket pursuant to HHS regulations at 45 CFR 46.407 and FDA regulations at 21 CFR 50.54.

1) **What are the potential benefits of the research, if any, to the subjects and to children in general?** Given the unquantifiable risk of smallpox exposure that is at this time small but greater than zero, the benefit to the subjects is immunity against smallpox. The benefit to children in general is an understanding of the efficacy and risks of smallpox immunization.

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- 2) **What are the types and degrees of risk that this research presents to the subjects?**
- a) The children in the study are likely to have limited, localized side effects (fever, pain, swelling, headache, nausea, fatigue, muscle aches).
 - b) There is a small risk of a significant adverse event (SAE) (disseminated vaccinia, eczema vaccinatum, encephalitis, keratitis). The SAE can be treated (except for keratitis and encephalitis) with vaccinia immune globulin (VIG) and sufficient amounts of VIG are currently available to treat the number of children who would be studied in the proposed protocol. The risk of SAE in the general (unscreened) population is approximately 15 per one- million. The population in the research study will be pre-screened.
- 3) **Are the risks to the subjects reasonable in relation to the anticipated benefits, if any, to the subjects, and the importance of the knowledge that may reasonably be expected to result?** While an accurate assessment of risk is difficult for public health officials to know with any degree of certainty, the information from the federal government can be construed to indicate that the risk of a terrorist incident is real. Coupled with the possibility that the government may make smallpox immunization available to the general public, the benefit from smallpox immunization to the child and knowledge from such immunization for children in general is great. Specifically, we need to determine efficacious dose and safety in children in the event that immunization is necessary or offered.
- 4) **Does the research present a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children?** Again, given the risk of a smallpox incident or the risks inherent in offering smallpox to the general population without first determining the efficacious dose in children, we believe there is great opportunity to learn from this clinical trial to further the understanding, prevention and alleviation of a serious health risk for children.

Sincerely,



E. Stephen Edwards, MD, FAAP
President

ESE/mc

¹ "Smallpox Vaccine" Committee on Infectious Diseases. *Pediatrics* Vol. 110(4):1-5.