§ 630.11 Clinical trials to qualify for license.

To qualify for license, the antigenicity of the vaccine shall have been determined by clinical trials of adequate statistical design conducted in compliance with part 56 of this chapter, unless exempted under § 56.104 or granted a waiver under § 56.105, and with part 50 of this chapter. Such clinical trials shall be conducted with five lots of oral poliovirus vaccine that have been manufactured by the same methods. Type specific neutralizing antibody for each type of poliovirus in the vaccine shall be induced in 90 percent or more of susceptibles after a series of doses.

§ 630.12 Animal source and quarantine; personnel.

(a) *Monkeys*—(1) *Species permissible as source of kidney tissue.* Only Macaca monkeys, Cercopithecus monkeys, or other species found by the Director, Center for Biologics Evaluation and Research, to be equally suitable, which meet the requirements of § 600.11 (f)(2) and (f)(8) of this chapter, shall be used as the source of kidney tissue for the manufacture of Poliovirus Vaccine Live Oral Trivalent.

(2) *Experimental and test monkeys.* Monkeys that have been used previously for experimental or test purposes shall not be used as a source of kidney tissue in the processing of vaccine.

(3) *Quarantine; additional requirements.* Excluding deaths from accidents or causes not due to infectious diseases, if the death rate of any group of monkeys being conditioned in accordance with § 600.11(f)(2) of this chapter exceeds 5 percent per month, the remaining monkeys may be used for the manufacture of Poliovirus Vaccine Live Oral Trivalent only if all of the monkeys survive a new quarantine period.

(b) *Personnel.* All reasonably possible steps shall be taken to ensure that personnel involved in processing the vaccine are immune to all three types of poliovirus and do not excrete poliovirus.

[56 FR 21432, May 8, 1991; 56 FR 27787, June 17, 1991]

§ 630.13 Manufacture of Poliovirus Vaccine Live Oral Trivalent.

(a) *Virus passages.* Virus in the final vaccine shall represent no more than five tissue culture passages from the original strain or no more than five tissue culture passages from a virus clone derived from one of the first five tissue culture passages of the original strain.

(b) *Virus propagated in primary monkey kidney cell cultures*—(1) *Continuous cell lines.* When primary monkeys kidney cell cultures are used in the manufacture of poliovirus vaccine, continuous cell lines shall not be introduced or propagated in vaccine manufacturing areas.

(2) *Identification of processed kidneys.* The kidneys from each monkey shall be processed separately. The resulting viral fluid shall be identified as a separate monovalent harvest and kept separately from other monovalent harvests until all samples for the tests prescribed in paragraphs (b)(3) and (b)(4) of this section relating to that pair of kidneys have been withdrawn from the harvest.

(3) *Monkey kidney tissue production vessels prior to virus inoculation.* Prior to inoculation with the seed virus and at least 3 days after complete formation of the tissue sheet, the tissue culture growth in vessels derived from each pair of kidneys shall be examined microscopically for evidence of cell degeneration. If such evidence is observed, the tissue cultures from that pair of kidneys shall not be used for poliovirus vaccine manufacture. To test the tissue found free of cell degeneration for further evidence of freedom from demonstrable viable microbial agents, the fluid shall be removed from the cell cultures immediately prior to virus inoculation and tested in each of four culture systems:

(i) Macaca monkey kidney cells,

(ii) Cercopithecus monkey kidney cells,

(iii) Primary rabbit kidney cells, and

(iv) Cells from one of the systems described in § 630.18(a)(6).

The fluid shall be tested in the following manner: Aliquots of fluid from each vessel derived from the same pair of kidneys shall be pooled and at least 10 milliliters of the pool inoculated into each system. The dilution of the