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“New High-speed Jet Injectors for Mass Vaccination: Pros and Cons of Disposable-cartridge Jet Injectors (DCJIs) versus Multi-use-nozzle Jet Injectors (MUNJIs)”

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Definition and Invention

Needle-free jet injection is a means of administering parenteral vaccines and other medications by use of a moving piston to compress liquid in an enclosed dose chamber, thus forcing it out a small orifice at high pressures sufficient to penetrate skin and reach targeted intradermal, subcutaneous, or intramuscular tissue. Jet injectors (JIs) were invented in the 1860s in France, for a therapy termed *l'aquapuncture*, *l'hydropuncture*, or *douches filiformes*. The technology was “rediscovered” in the U.S.A. in the 1930s upon observation of hydraulic fluid in a worker’s hand without obvious point of entry which resulted from a pinhole leak in a hydraulic line. The first patents were issued in the 1940s.

Slow-speed Devices for Personal Use

The first commercial device, the Hypospray[®], was promoted in the late 1940s for use by individual diabetics to overcome needle-phobia over frequent insulin injections. This indication remains today the basis for a small niche market of slow-speed JIs (e.g., the AdvantaJet[™], CoolClick, GentleJet[™], Injex[™], J-Tip[®], Medi-Jector[®], SeroJet[™], and Vitajet[®], *inter alia*) for use only by the same patient for self-injection of insulin and, more recently, other drugs requiring frequent injection, such as human growth hormone. See: <http://www.cdc.gov/nip/dev/jetinject.htm>

High-speed Devices Classified as MUNJIs

In the 1950s, jet injection was adapted under military contract to develop the high-speed Ped-O-Jet[®] for use in mass vaccination of recruits. Dr. Robert Hingson (1913-1996) was instrumental in the research, development, and clinical studies of such high-speed devices for mass vaccination, as well as the personal JIs for self-injection mentioned above. The Ped-O-Jet[®] and many similar devices (e.g., the BIP-4[™], Dermo-Jet[®], Hypospray[®] Professional and K3 models, Im-O-Jet[®], Med-E-Jet[®], and SICIM[™], *inter alia*) are filled by suctioning vaccine into their dose chambers from attached large, multi-dose vaccine vials of 25 mL volume or more. They are capable of 600 to 1000 injections per hour. Because the same nozzle and fluid pathway are used for consecutive patients, existing high-speed devices are classified here as **multi-use-nozzle jet injectors** (MUNJIs). Since the 1950s, MUNJIs have delivered literally billions of doses of vaccine in mass campaigns around the world to prevent influenza, measles, meningococcus A and C, polio, smallpox, and yellow fever, among other target diseases.

Safety Concerns for MUNJIs

In the 1980s, a Med-E-Jet[®] MUNJI was implicated in an outbreak of several dozen cases of hepatitis B in California. Subsequent bench studies of it and the more common Ped-O-Jet[®] indicated that their nozzles could become contaminated with hepatitis B virus and pose a risk for transmission between

consecutive vaccinees. In the 1990s, a variety of other bench laboratory, animal model, and field epidemiologic studies resulted in concern for potential transmission of bloodborne pathogens to subsequent vaccinees by such MUNJIs. These included studies of ejected vaccine doses collected during actual vaccination campaigns in Brazil (de Souza Brito, *et al.*, <http://www.aegis.com/conferences/10wac/pc0132.html>), an animal model for safety evaluation developed in the United Kingdom (Hoffman PN, *et al.*, *Vaccine*, 2001;19:4020-4027 http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11427278), and a statistically significant association between hepatitis B infection and having been vaccinated by MUNJI (Souto FJ, *et al.*, *Rev Panam Salud Pública* 2001; 10:388-394 http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11820107&dopt=Abstract). In 1997, the manufacturer of the Ped-O-Jet[®] withdrew them and their spare parts from the market because of concern for legal liability, prompting the U.S. military to suspend their use (<http://www.cdc.gov/nip/dev/jetinject.htm#policies>) Currently, WHO recommends against MUNJI use until they are proven safe. CDC policy limits MUNJI use to urgent situations in which the benefits of speed outweigh the risks.

Unpreparedness for mass vaccination

As a result of the limbo status for MUNJIs, public health agencies lack a high-speed vaccination device of unquestioned safety for parenteral vaccines. This leaves them vulnerable to manpower constraints and risks of using needles for disease control and eradication goals (e.g., measles), global and regional epidemics (e.g., influenza, future SARS vaccine), and bioterrorism (e.g., anthrax). Two parallel efforts are underway to overcome this vulnerability: (1) re-engineering of the MUNJI technology to make it safer, and (2) research and development of high-speed *disposable-cartridge jet injectors* (DCJIs).

Re-engineered MUNJIs

Felton Medical International, Inc. (Lenexa, Kansas, USA), with financing from the U.S. Department of Energy for U.S.-Russian technology cooperation, and with assistance from PATH (Seattle, USA), is applying long-term experience and designs from the Russian MUNJI industry to use a new disposable, auto-disabling safety cap on a new BI-100[™] model. The cap would contain any splash back from the patient that might contaminate the next injection. One advantage of this method is that the injector draws directly from large multi-dose vials mounted atop the injector, and is capable of the same 600-1000 injections per hour as the old MUNJIs. A major obstacle for this approach is that there remains no validated *in vivo* or *in vitro* methodology of sufficient sensitivity, specificity, repeatability and overall rigor for regulatory review of the safety of re-engineered MUNJIs in order to permit or recommend their use. Indeed, the currently presumed minimal infectious volume of blood capable of transmitting highly-infectious hepatitis B (10 pL) is based on a single titration study from an infected chimpanzee, which may be off by an order of magnitude or more. Another difficulty is to prevent end users from defeating the auto-disabling feature of the safety caps that might permit repeated injections with the same cap, or even no cap at all. Nightly field sterilization of the MUNJI would be required during mass campaigns.

Disposable-cartridge Jet Injectors (DCJIs)

In the 1990s, several slow-speed DCJIs were introduced in North America, Europe, and elsewhere, including the Biojector 2000[®] targeted for immunizations and other devices for the insulin market (cited above, ¶2). Building on this concept, D'Antonio Consultants International (East Syracuse, New York, USA), with financing from CDC, is developing a DCJI system suitable for both high-speed and routine vaccination settings. Its advantages include an autodisable disposable cartridge capable of both manufacturer prefilling, as well as clean field filling by end-users from multi-dose vials with a separate filling station. A motorized LectraJet[®] powered by rechargeable batteries is capable of >600 injections per hour without undue operator fatigue. A manually-cocking model would function just as fast. Cartridges would be supplied in 30-dose magazines for fast fingers-free loading and unloading onto

and off the injector. Fewer numbers of doses could be filled and/or injected without affecting the sterility of remaining manufacturer-prefilled doses or empty cartridges to be filled by end users another day. Estimated cost for sterile and wrapped magazines is approximately U.S. \$0.06 per cartridge. Obstacles include convincing manufacturers to prefill vaccines into such cartridges, and ensuring that end-user filling of sterile, empty magazines would be clean and safe. Another challenge is to create a universal standard for such cartridges with enlightened intellectual property licensing to permit a healthy competitive market among manufacturers of disposables, vaccines, and DCJIs.