

K960285

**510 (k) Summary of Safety and Effectiveness
for the
Medi-Jector Needle-Free Bio-Tropin™ Drug Delivery System**

Final Manufacturer/510(k) Submitter:

Medi-Ject Corporation
1840 Berkshire Lane
Minneapolis, MN 55441

Official correspondent/contact person:

Peter Sadowski, Ph.D.
Vice-President of Product Development
Tel.: (612) 551-4177
Fax: (612) 553-1610

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Device Trade/Proprietary Name: Medi-Ject Corporation Medi-Jector Needle-Free
Bio-Tropin™ Drug Delivery System
Common/Usual Name: Fluid injector
Classification Name: Non-electrically powered fluid injector (21 CFR
880.5430)

This summary is provided to detail the safety and effectiveness information used to support a finding of substantial equivalence of the Medi-Jector Needle-Free Human Growth Hormone Injection System to the Medi-Ject Corporation Medi-Jector IV(EZ) and Medi-Jector V (TT) Needle-Free Insulin Injection Systems, the subjects of 510(k)s K864561 and K883847, respectively, and to the Bioject Inc., Biojector 2000 Needle-Free Injection Management System, described in 510(k) K920631.1

The Medi-Jector Needle-Free Human Growth Hormone Injection System is a needle-free, spring-powered human growth hormone (hGH) injection system. It is comprised of a "power pack" with a detachable nozzle. The power pack contains the spring and has a plastic housing, injection release button, safety latch, and dosage display window; it is wound to draw up the desired dose of reconstituted hGH (up to 0.5 ml of hGH in bacteriostatic saline). The reusable stainless steel nozzle is supplied non-sterile and requires cleaning and boiling sterilization by the user prior to first use and every two weeks thereafter. The device is intended only for the long-term treatment of children who have growth failure due to an inadequate secretion of normal endogenous growth hormone. It is intended for the subcutaneous administration of the reconstituted drug by high-pressure injection either by health care practitioners or directly by patients. The device is not supplied pre-loaded with hGH; rather, it utilizes a supplied sterile "bottle adapter" accessory, with an integral spike, to aseptically penetrate the rubber seal of a standard vial of reconstituted hGH, accept the Medi-Jector's nozzle end, and thus draw a calibrated dose of reconstituted hGH into the chamber of the opaque nozzle assembly by way of winding motion of the power pack.

1 The Biojector 2000 with CO₂ cartridge power source entered commercial distribution without the filing of a premarket notification or finding of substantial equivalence. It was initially described to FDA in subsequent K920631 seeking addition of an adapter to allow connection to a CO₂ tank.

Upon deactivation of the safety (latch) switch, and pressing of the proximal injection release button, pressure from the power pack's spring is exerted on a plunger within the nozzle, forcing the liquid reconstituted hGH through a small orifice (0.0058" or 0.0068" diameter) in the distal part of the nozzle and simultaneously transforming it into a liquid column. An intense and almost instantaneous pressure pulse allows the drug to penetrate the patient's skin, where it is disbursed within the subcutaneous tissue. The depth of penetration is determined by the power of the spring, the nozzle orifice diameter, and a winding adjustment of the power pack executed between the times of drawing the drug dose and injection.

The Medi-Jector Needle-Free Bio-Tropin™ Drug Delivery System is identical to the predicate Medi-Jector IV (EZ) and V (TT) Needle-Free Insulin Injection Systems with the exception of outer power pack plastic housing and button/switch materials, power pack diameter (approx. 0.2 in. larger), power pack spring force at full compression (80-85 lbs. vs. 105-110 lbs or 80-90 lbs, respectively), dosage display (ml hGH vs. units of U-100 insulin) and intended use (injection of reconstituted hGH instead of U-100 insulin). The Medi-Jector differs from the Biojector 2000 mainly in the energy source used to propel a plunger to expel the medication out a micro-orifice at high velocity (spring vs. CO₂ cartridge), method of drawing drug (bottle adaptor vs. detachable syringe and fill needle), use of a reusable stainless steel nozzle/plunger and injectate capacity (0.5 ml vs. 1.0 ml). As demonstrated by in vitro performance testing (see below), there are no differences in technological characteristics affecting safety or effectiveness. The Medi-Jector's intended use for subcutaneous hGH injection is a subset of the Biojector's use in injecting vaccines and other injectable drugs intramuscularly or subcutaneously.

Safety and effectiveness information supporting a claim of substantial equivalence included sterility, biocompatibility, performance data, and clinical testing.

Sterility data was based on validation of the methods utilized to assure the sterility of the Medi-Jector's bottle adaptor and the Biojector's syringe and fill needle which contact medication in its sterile vial. The Medi-Jector bottle adaptor was validated to a sterility assurance level of 10⁻⁶.

Biocompatibility was evaluated on all Medi-Jector materials contacting the medication; this testing included a study comparing the acute subcutaneous tolerance of pigs to Medi-Jector versus standard syringe/needle injection. In the case of the Biojector, patient and/or medication-contacting components had been tested per Tripartite Biocompatibility Guidelines. The biocompatibility of the Medi-Jector's drug-contacting materials was verified and it was concluded that there were no differences in macroscopic or microscopic porcine dermal alterations over 72 hours after the Medi-Jector or standard needle injection.

In vitro testing included evaluation of the effect of Medi-Jector injection and bottle adaptor contact on the biochemical integrity of the hGH molecule, evaluation of the compatibility of hGH with the Medi-Jector injection nozzle friction seals, and power pack ink printing rub resistance testing. There was no evidence that Medi-Jector injection changes the chemical integrity of the injected hGH molecule; at a power/penetration setting of "8" or at maximum power, there was no effect on the levels of dimers, oxidized forms, or deamidated forms of hGH, and no molecular differences between jet-injected and standard syringe/needle-injected hGH. An apparent hGH loss of 81.1-93.9% from Medi-Jector injection was believed to be an artifact of the experimental method. Spectrophotometric analysis did not reveal significant amounts of cadmium or lead leaching from adapter materials submerged in reconstituted hGH for up to 21 days at 5°C or 37°C; concentrations of these heavy metals were generally within the range of blank reference controls (isotonic saline). Chromatographic analysis of the adapter/hGH solution did not reveal any peaks different from the control hGH solution, even after 6 days of incubation at 4°C. Analysis of adapter parts incubated in reconstitute hGH at 5°C for up to 21 days did not demonstrate a progressive increase in the polymeric, deamidated, oxidized, or unknown forms of hGH or a difference from controls; at 37°C incubation, the deamidated, oxidized, and unknown forms of hGH increased over 21 days for both

test samples and controls, but sample levels remained equivalent to controls at all time points. Repeated fillings of the Medi-Jector with various dyes in bacteriostatic saline did not demonstrate moistening of the plastic and rubber friction seals in the Medi-Jector nozzle. There was no change in dimensional conformance, tear strength, or surface quality of the nozzle seals after exposure to hGH in bacteriostatic saline for up to 5 weeks at room temperature, or after 5 cycles of boiling in distilled water (the recommended cleaning method for the injection nozzle). The ink printing on the Medi-Jector power pack withstood 25 double rub cycles with a solvent challenged rubbing cloth applied with at least 2 lbs of force; the solvent challenges involved moistening the rubbing cloth with recommended cleaning solutions.

Performance testing of the Medi-Jector Needle-Free Bio-Tropin™ Drug Delivery System included pressure curve testing, comparison of penetration depth and dispersion in an artificial matrix to the Biojector 2000, delivery accuracy, and reuse durability. Pressure curve experiments confirmed the identity of this device with the proposed predicate devices. Penetration studies confirm similar penetration of injectate between the Medi-Jector and Biojector 2000. Firing bidistilled water at room temperature demonstrated a mean Medi-Jector error of 1.4% at a target dose of 0.125 ml and 0.37% at a target dose of 0.5 ml. The reuse durability testing supported the notion that extensive use of the devices does not significantly impact the volume delivery.

Because the bottle adapter accessory remains mounted on the hGH vial until it is empty, and because of the recommended Medi-Jector nozzle 2 week user disinfection interval, cleanliness issues were addressed by testing the potential of an attached sterile Medi-Jector bottle adapter to contaminate the vial of sterile reconstituted hGH and by evaluating the sterility of the Medi-Jector injection nozzle hGH-contacting parts between routine user boiling sterilizations. Vials of reconstituted hGH with mounted bottle adaptors and attached adaptor caps were soaked for 5 days at 5°C in 0.9% saline spiked with 1.85×10^6 organisms/ml of *Pseudomonas putida*, and the vial contents then incubated; the demonstrated absence of bacterial contamination showed that penetration of a vial of reconstituted hGH by the adaptor spike does not contaminate the drug, and validates the integrity of closure of the adaptor/vial combination closed with the supplied adaptor cap, preventing bacteria from entering the vial of hGH solution. After up to 28 days of simulated uses, including once-daily filling and discharge of the Medi-Jector with hGH and placing the nozzle against the patient's skin, it was concluded that once-daily use of the disinfected (steam-sterilized) Medi-Jector for hGH injection, with or without using the protective nozzle cap during device storage at room temperature (21°C), still ensures the hygienic status of the device's hGH-contacting nozzle components for at least 28 days, regardless of whether the skin is pre-wiped with isopropanol prior to Medi-Jector contact.

Clinical studies were conducted on 12 healthy young male volunteers, age 20-33, each of whom received two injections of reconstituted hGH (5 IU in 0.5 ml subcutaneously), once each with the Medi-Jector and by conventional syringe/needle, with treatment sequence in random order and at least a 7-day washout between drug administrations. The Medi-Jector was set at a penetration setting of "6" for each patient, although in normal clinical practice penetration would be set by the individual to obtain subcutaneous drug administration. Blood samples were obtained from each subject immediately pre-injection and on multiple occasions through 24 hours post-injection and analyzed for levels of hGH (somatotropin), IGF-I (somatomedin C) and free fatty acids. Over the 24 hour post injection observation periods for each of the two administration methods it was demonstrated that the systemic exposure to hGH, in terms of the amount of drug absorbed into the circulation, was similar (bioequivalent) for Medi-Jector and conventional syringe administration. A higher and more rapid onset of the hGH peak concentration was found after Medi-Jector administration, presumably due to a maximal spreading of the injection fluid with resultant enlarged surface area favoring drug absorption. A marked increase in IGF-I serum concentration (37.9% mean increase for Medi-Jector, 41.3% mean increase for syringe injection from injection time to 24 hours thereafter) was observed after hGH administration by the two treatments; no statistically significant difference in IGF-I between treatments was found at any time point measured during the 24-hour post-injection observation period (bioequipotency). Although the

same rhythmic variations in free fatty acids were observed after each treatment, the known stimulating effect of hGH on lipolysis was not demonstrated. Other than two mild skin lesions after incomplete Medi-Jector injection and one mild hematoma 24 hours after Medi-Jector use, there were no problems in the post-study evaluations and no serious adverse reactions. Because the incomplete Medi-Jector injections were probably due to the penetration setting ("6") set for all subjects, it was recommended that the device should be set individually for actual clinical use.

Another clinical study was cited in an included published report on use of the Medi-Jector for injecting growth hormone in hGH-deficient children (Igarashi Y, Okuno A, Sto Y, et al: "Use of a jet valve type needle-less injector for growth hormone therapy", Clin. Rep. 27:5951-5961, 1993). This study concluded that height increase and improvement in growth rate were comparable among hGH-deficient children receiving hGH by Medi-Jector or syringe injection. (Note any complications)

The above non-clinical and clinical testing demonstrates that the Medi-Jector Needle-Free Human Growth Hormone Injection System is as safe and effective, and performs at least as well as the noted predicate devices, and thus justifies a determination of substantial equivalence.