Early this year, Lexington International Inc.’s HairMax LaserComb became the first medical device for promoting hair growth legally marketed in the United States. The clearance received considerable national publicity as the popular press focused on the human interest stories surrounding this hair growth product. This article presents a case study of how Lexington, with help from the law firm King and Spalding, obtained premarket clearance from the Food and Drug Administration (FDA) by overcoming significant regulatory obstacles.

The HairMax LaserComb is an over-the-counter (OTC) device that FDA has cleared “to promote hair growth in males with androgenetic alopecia who have Norwood-Hamilton Classifications of IIa to V and Fitzpatrick Skin Types I to IV.” In other words, the HairMax LaserComb is indicated for use by men with minor to moderate hereditary baldness who have light to medium skin tones. The HairMax LaserComb is a hand-held, low-level laser device. The patient-contact surface of the device consists of a row of laser lights with two rows of comb teeth on either side of the lights. The HairMax LaserComb delivers laser light to the scalp to stimulate hair follicles. The comb teeth part the user’s hair to form a clear path for the light to reach the scalp.

There are two primary regulatory paths for obtaining FDA authorization to market medical devices: clearance of a 510(k) premarket notification, or approval of a premarket approval (PMA) application. The vast majority of new devices are cleared through the 510(k) process. To obtain 510(k) clearance, a new device must be “substantially equivalent” to at least one legally marketed predicate, which is a device that either 1) has already received 510(k) clearance; or 2) does not require 510(k) clearance because a) it was on the market prior to the May 28, 1976, enactment of the Medical Device Amendments to the federal Food, Drug, and Cosmetic Act (FDCA) and, thus, is “grandfathered,” or b) it is exempt from 510(k) requirements.

A new device is substantially equivalent to a predicate device if it has: 1) the same intended use, e.g., treatment of baldness; 2) the same indications, e.g., promoting hair growth, or any differences in the new device’s indications do not affect its therapeutic or diagnostic purpose; and 3) the same technological characteristics, e.g., laser beam and comb components, or its technological differences do not raise new questions of safety or effectiveness, and performance (bench, animal or human) data demonstrates that the new device is as safe and effective as the predicate device(s).

FDA can require clinical (human) data whenever there are differences
between the new device and its predicate(s). In addition, FDA can easily find that differences in a device’s indications affect its therapeutic or diagnostic purposes, and/or that its technological differences raise new questions of safety or effectiveness and, thus, require a PMA. Therefore, FDA has broad discretion whether to clear a device that is not identical or nearly identical to its predicate device(s) even if the 510(k) notice includes clinical data.

The HairMax LaserComb 510(k) notice included a complex predicate device comparison and clinical data.

Predicate Device Comparison

Prior to the submission of the 510(k) premarket notification for the HairMax LaserComb, FDA told Lexington that the agency had never cleared (or approved) a device for hair growth and, thus, there was no direct predicate for the HairMax LaserComb. For this reason, FDA expressed doubt that it could find this device to be substantially equivalent even if the 510(k) notice included clinical data.

The lack of a direct predicate device meant that Lexington and King & Spalding had to compare key features of the HairMax LaserComb to different predicate devices. In addition, Lexington had to be creative to find such predicates. The company determined that devices for treating baldness that were marketed before FDA began regulating medical devices were the only possible predicates with a similar indication. Lexington searched late nineteenth and early twentieth century magazines and newspapers online for examples of such products. For each of the HairMax LaserComb’s primary technological characteristics, Lexington identified a generic type of device that had similar characteristics. The company then searched the 510(k) database on FDA’s website and the trade press for specific devices within each of those generic types, and found the following predicate devices for the HairMax LaserComb:

- Grandfathered instruments for treating baldness, including “Dr. Scott’s Raydo and Wonder Brushes,” to show that hair growth is not a new indication for devices;
- Lasers that FDA has cleared for hair removal to show that the agency has already determined that laser light affects hair growth;
- Lasers that FDA has cleared for therapeutic indications other than hair growth, i.e., wrinkle treatment and temporary pain relief, with the same wavelength as the HairMax LaserComb or with a range of wavelengths that encompassed the HairMax LaserComb’s wavelength to demonstrate that this feature does not raise new safety issues; and
- Cleared lice and psoriasis combs to show: 1) the delivery of energy (heated air and radiation, respectively) to the scalp for a therapeutic purpose was not a new indication; and 2) the use of comb teeth to part the hair to direct the energy to the appropriate location was not a new technological characteristic.

Thus, Lexington and King & Spalding compared the HairMax LaserComb to a combination of predicate devices.

FDA did not ask any questions regarding Lexington’s predicate device comparison during the agency’s review of the 510(k) notice. The company interpreted FDA’s silence to mean that the agency concluded that the HairMax LaserComb, while not a “me-too” device, was enough like its predicate devices for it to be 510(k)able, although clinical data is required. Thus, this comparison served its intended purpose.

Clinical Data: Counting Hairs

Lexington conducted a multi-center, randomized, placebo-controlled clinical study in the United States. Subjects used either the HairMax LaserComb or a sham version of the device that looked identical to, and appeared to function in the same way as, the HairMax LaserComb, but which did not contain a laser. Thus, subjects were “blinded” to whether they received the active or the placebo device. Subjects were instructed to use the device three times per week on non-consecutive days for a total of 26 weeks.
At the beginning and at the end of the six-month study, trained observers counted the number of terminal (thick) hairs in each subject’s treatment area using images of the subject’s head. The HairMax LaserComb subjects experienced a mean increase of 18.8 thick hairs per centimeter squared (cm$^2$), which is about the size of a dime, compared to a mean decrease of 10.6 hairs/cm$^2$ for the placebo group. This difference was statistically significant. Moreover, 93.1 percent of HairMax LaserComb subjects compared to 12.5 percent of the placebo subjects had some increase in hair density. Thus, the hair count data showed that the HairMax LaserComb promotes hair growth.

In addition, a significantly larger percentage of subjects in the HairMax LaserComb group reported some hair growth after six months of treatment compared to subjects in the placebo group. However, the clinicians participating in the study (“investigators”) did not find a statistically significant difference in the percentage of subjects in HairMax LaserComb and the placebo groups who experienced hair growth based on global photographic assessments. (This assessment is dependent on a number of variables, including hair length, hair style, hair part, whether the hair is wet, background color, exposure, and lighting). Thus, the subjects and the investigators had different perceptions regarding the efficacy of the HairMax LaserComb.

None of the study subjects experienced a serious adverse event. In addition, the types and number of adverse events were similar between the two groups. Thus, the clinical study clearly demonstrated the relative safety of the HairMax LaserComb.

As discussed in more detail below, the clinical studies of the first drug approved for promoting hair growth had the same challenges regarding investigators’ global assessments.

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Objective v. Subjective Data

FDA generally prefers objective data, such as quantitative measurements, to subjective data, such as qualitative assessments. The primary efficacy endpoint for the HairMax LaserComb clinical study was an objective measurement since it involved observers counting the number of hairs in the treatment area that met certain predefined criteria. In this case, the objective data clearly demonstrated that HairMax LaserComb subjects experienced more hair growth than subjects in the placebo group.

The subjects’ and the investigators’ assessments of hair growth were both subjective endpoints because they simply characterized their own or each subject’s hair growth, respectively, as “no growth,” “minimal growth,” “moderate growth,” or “dense growth.” The subjects’ assessments, unlike the investigators’ assessments, were consistent with the objective data. This result suggests that that the subjects’ assessments were more accurate than the investigators’ assessments. In addition, the subjects’ assessments arguably are more important than the investigators’ assessments because 1) hair growth is primarily a cosmetic benefit, and 2) the subject obtains this benefit only if he sees an improvement. Nevertheless, the investigators’ equivocal assessments concerned FDA, presumably because the agency perceived them as neutral experts. Therefore, FDA requested that Lexington explain why the agency should clear the HairMax LaserComb based on the existing clinical data.

Responding to FDA’s Request

In response to FDA’s request, Lexington explained that the clinical data supported clearance of the HairMax LaserComb based on three grounds.

First, FDA’s longstanding policy is to clear or approve a device (or a
drug) if it meets its primary efficacy endpoint even if it does not meet all of its secondary efficacy endpoints. The company pointed out that, in general, FDA is especially willing to uphold that policy if the primary efficacy endpoint is objective and the secondary endpoints are subjective. In this case, the HairMax LaserComb met its sole primary endpoint, and this endpoint, unlike its secondary endpoints, was an objective measure.

Second, Lexington asserted that FDA had already established the rules for interpreting clinical data for products that promote hair growth. Lexington explained that the company deliberately, with FDA’s concurrence, designed the clinical study of the HairMax LaserComb to mirror the two clinical studies on which the agency based its approval of the first drug for promoting hair growth. Therefore, both sets of studies had the same primary efficacy endpoint, i.e., hair count, and the same secondary efficacy endpoints, i.e., subjects and investigators’ global assessments of hair growth. In addition, the results of the HairMax LaserComb clinical study were at least as positive as the results of the drug studies because 1) the treatment group had a statistically significant increase in mean hair count compared to the placebo group for both products; 2) significantly more subjects in the treatment group than the placebo group in the HairMax LaserComb study and in one of the two drug studies reported hair growth; and 3) the investigators did not find a statistically significant difference in the percentage of subjects in the treatment and control groups who experienced hair growth at the end of the HairMax Laser Comb study and one of the drug studies. Moreover, FDA approved that drug solely because it met its primary efficacy endpoint. Thus, Lexington asserted that FDA’s approval of that drug serves as precedent for the agency’s clearance of the HairMax LaserComb based on its existing clinical data even though 1) the drug in question is not a predicate for the HairMax LaserComb, and 2) the results of their clinical studies cannot be directly compared because Lexington did not conduct head-to-head testing of the products.

And, finally, Lexington and King & Spalding emphasized that the HairMax LaserComb, unlike a drug for promoting hair growth, does not present any significant safety issues. These three arguments apparently convinced FDA to clear the HairMax LaserComb for promoting hair growth. Thus, Lexington successfully used FDA’s policies, precedent, and past practices to eliminate the agency’s initial skepticism about the clinical data.

**Conclusion**

Lexington obtained 510(k) clearance for the HairMax LaserComb despite two significant regulatory hurdles: 1) the lack of a direct predicate device, and 2) clinical data that was primarily, but not entirely, positive. Lexington succeeded where many other companies would have failed because it thoroughly understood FDA’s 510(k) requirements, was creative in meeting those requirements, and was responsive to the agency’s requests for additional information.

Few 510(k) notices have as difficult a regulatory path as the HairMax LaserComb. However, this extreme example highlights the basic approach for all 510(k) notices and provides some insight on preparing and managing more complex submissions. △