

Excerpts from Analyst's Report, October 19, 2009

NOBN is symbol for Nobel Biocare, referred to herein as "Nobel"
(Emphasis and Links Added)

Overview:

- 1. Nobel's implant packaging has failed a standard dye leak test, suggesting a potential breach in ongoing sterility.*
- 2. The FDA could institute a product recall, which would be a serious problem for Nobel.*

Summary:

Industry participants think that Nobel could be facing a major problem with the integrity of its implant packaging. **Based on independent dye immersion tests conducted and detailed by one of its competitors (we have also seen similar results from a separate, independently commissioned test), it appears that the vials that house Nobel implants may fail to maintain a sterile seal.** This could be a serious issue since Nobel implants are labeled as "sterile" when they are shipped. **A contaminated implant could result in implant failure and or patient infection. The "information for use" statement accompanying Nobel's implants clearly states that the product should not be used if the package has been damaged or previously opened.**

Nobel has been made aware of this issue, which has only recently been made public on a competitor's web site. Its response to date has been a denial, of sorts, that there is a problem. Nobel recently sent a letter to its customers addressing the claims of its competitor. In the letter, it states that Nobel products meet all required quality and safety standards and notes that a recent independent external review reported no quality issues with Nobel products. Lastly, it claims that it has "the necessary data to establish that its products are safe and maintain sterility." **However, as far as we know, it has yet to publicly show this data, nor has it publicly confirmed that it has conducted additional tests (dye immersion; microbial challenge) on its implants.** If it had such data, it would seem sensible to disclose it immediately, considering the potential ramifications of the accusation.

Interestingly, **the company does not outwardly appear to refute specifically the results of the dye test. Rather, it states that it is not an "appropriate test" to confirm the maintenance of sterility of its products. Nevertheless, industry experts, with whom we have spoken, disagree,** as we explain in the report. While Nobel's initial testing methods (at the time of packaging) might demonstrate that the product is sterile, **the company has, to our knowledge, provided no evidence that its packaging maintains the integrity of the closure system throughout the duration of the indicated 5-year shelf life, as required by ISO 11607.** Moreover, the fact that its implants failed a standardized dye leak test raises the question of the validity of Nobel's own testing methods. The issue is not what test Nobel used in its FDA 510k submission, but whether the vials maintain an adequate seal to assure that the contents remain sterile. When we inquired, the company would not disclose to us the method it used to confirm continuous sterility of its product, nor would it name the entity that conducted the "external review."

Nobel has faced similar issues in the past. As we discuss in the report, it received a warning letter from the FDA in 1992 due to "serious violations in Good 3 Manufacturing Practices." Among other things, the FDA cited its sterilization procedures as well as a "failure to investigate, after a device has been shipped, any failure of that device to meet performance specifications." As a result, Nobel's implants

were banned from being imported into the U.S. and Nobel lost a meaningful percent of market share. In 2008, the FDA finalized guidance regarding "container and closure system integrity testing as a component of the stability protocol for sterile products." It states that sterility testing at the initial time point is not considered sufficient to demonstrate the microbial integrity of a container closure system, and that physical testing, including dye leakage tests or microbial integrity tests can be used to verify that the seals are continuously leak free. Further more, the guidance goes on to state that manufacturers of medical devices "must validate" processes, including sterilization for a device purporting to be sterile. We have been told that the FDA has been officially notified of the independent dye leak test results. While it is uncertain when, if, and to what degree the FDA might require Nobel to rectify the problem, it seems likely that the agency would take some action.

Discussion:

We are fully aware that Dr. Niznick has been a vocal opponent of high priced implants and has an economic incentive to gain market share at the expense of a large competitor. Dr. Niznick, who is considered one of the founders of the dental implant industry, sold his former implant company in 2001 to a company later purchased by Zimmer. He started Implant Direct (in 2004 and started selling products) shortly after his non-compete clause expired in January 2006. **By eliminating most of the sales and marketing costs, Implant Direct offers a full range of comparable (and possibly superior) dental implants at a 50%-65% discount to the typical price of the major implant manufacturers. It is important to note that Nobel appears to have fired the first shot in this skirmish by allegedly using questionable tactics to discredit Implant Direct,** as we discuss in the report. Regardless, we think the public dissemination of his findings could have serious negative consequences for Nobel.

Following a series of events, which we discuss later in the report, Dr. Niznick commissioned an independent test of three Nobel implants (1 Nobel Replace and 2 Nobel Active). The detailed descriptions of the tests and the results are public information and have been posted on the Implant Direct website. The tests were conducted by Nelson Laboratories (an accredited independent lab in Salt Lake City), in accordance with USFDA and USEPA regulations. **According to the test results, all 3 of the Nobel implants showed significant dye penetration into the vials and thus failed** ASTM D4991-94: "Standard Test Method for Leakage Testing of Empty Rigid Containers." This is a standardized dye leak test commonly used for gamma radiated medical devices. **Importantly, Nelson also performed the same test on six Implant-Direct implants - none of which showed any signs of leakage.** These test results indicate that Nobel's "sterile" implant packaging may not provide an effective microbial barrier under all conditions. Therefore, it could be considered as failing to perform as specified and potentially contributing to real or potential patient harm.

We also became aware of an identical test, using the same lab, and using the same types of implants, that was commissioned by an independent party, not connected in any way to Nobel or to Implant Direct. We have the original results of that test and the testing materials themselves. The results of this test mirror those of the test conducted by Nelson Labs for Implant Direct.

According to **a summary report recently filed (with the FDA) by Implant Direct,** in January 2007, during the course of an evaluation of its implant packaging, Implant-Direct conducted container and closure integrity testing on its implants. It included in these tests, two samples of Nobel implants, marked as "sterile". **Both Nobel samples failed the test, as evidenced by the presence of dye** within the vial. Implant-Direct did not act on this information at the time. However, in June 2009, Implant Direct Canada demoted its Director of Operations, Ms. Adele Fussi, to a sales position. She resigned and applied for a position with Nobel Biocare, during which time she reported Implant-Direct to Health Canada regarding a packaging issue experienced two years earlier.

This resulted in an inquiry that has since been resolved. The issue related to a small number of [implants with a cosmetic micro-crack in the plastic cap that were removed from inventory](#). **Only 7 implants were actually recalled from Canadian dentists and exchanged.** When Ms. Fussi and her sales managers at Nobel began to contact Implant-Direct customers with information regarding the recalled implants, Implant Direct initiated litigation that is now pending in Canada.

According to the same report, in August 2009, Implant Direct arranged for a practitioner to order 2 NobelActive and 1 NobelReplace implants and sent these to an FDA approved independent lab for leak testing. [The results of all three tested samples showed significant dye penetration into the vials](#). Dr. Niznick next reportedly approached the General Manager of Nobel Biocare NA with these latest independent test results. His response reportedly was that a dye leak test was not the appropriate sterility integrity test for Nobel's packaging. Finally, [Dr. Niznick reportedly sent an email to the CEO of Nobel detailing the regulatory requirements for sterility containment testing](#), including establishment of the validity of the test method. Following a similar response, [Dr. Niznick presented this information to the FDA in a Medwatch Report, and posted it on his company's website](#).

We reviewed the FDA's recently finalized guidance on Container and Closure System Integrity Testing in Lieu of Sterility Testing as a Component of the Stability Protocol for Sterile Products. It provides guidance to manufacturers of various sterile products (including medical devices) for using methods other than sterility testing to "confirm" container and seal integrity. Products labeled as sterile are expected to be free from viable microbial contamination throughout the product's entire shelf life (5 years in the case of NOBEL implants). Moreover, sterility testing at the initial time point is not considered sufficient to demonstrate the microbial integrity of a container closure system -"the purpose of stability testing is to provide evidence on how the quality of a product varies with time under the influence of a variety of environmental factors ...sterility tests for the purpose of demonstrating continuing sterility have limitations, with respect to the method's reliability, accuracy, and the conclusions that may be derived from the results ... alternative methods may be more reliable in confirming the integrity of the container and closure system." **The guidance goes on to state that manufacturers of medical devices "must validate" processes, including sterilization for a device purporting to be sterile, and that an appropriate integrity test should be conducted "annually and at expiration."** While we are not in a position to speculate whether or not Nobel has conducted the appropriate tests to confirm the integrity of its implant containers, it has so far, to our knowledge, provided no tangible evidence of doing so, despite repeated inquiries.

[On 9/24/09, Kevin Mosher \(President of Nobel Biocare North America\) sent a letter to Nobel customers to assure them of the safety of its products.](#) We are unaware of any evidence that Nobel has provided to support its claim that its products meet all required quality and safety standards. We asked Nobel if it has conducted such tests and we were told that the company does not provide information on its testing methodologies. We spoke with top-level industry people from several different medical device packaging companies. We also spoke with container testing experts from several different ANSI/ISO accredited labs. Based on those discussions and the results from the failed dye leak tests, we think it's reasonable to question the validity of any tests used by Nobel to validate its shelf-life claims.

While we cannot know what, if any, test was conducted by Nobel to demonstrate the ongoing maintenance of seal integrity and package sterility we assume that the company has conducted some alternative test and that its packaging passed that test. If that is the case, the company might argue that its test alone is sufficient to confirm the integrity of its packaging and that a dye leak: test is not an appropriate test. That would then put the matter into the hands of the FDA to decide whether a package

that is labeled as sterile and has been shown to leak under certain conditions meets current standards of safety. **However, the experts with whom we spoke were nearly unanimous in their belief that the failed dye tests are enough to suggest that another testing methodology has to be questioned and that the Nobel implant packaging system that failed the dye tests would probably have to be replaced.** One packaging insider noted that, since implants from two different factories were included in the aforementioned tests, it suggests that there is a flaw in the design of the packaging system and not a process or machine problem.

Nobel has had problems in the past with its quality control. In February 1992, the FDA issued a warning letter to Nobel due to "serious violations in Good Manufacturing Practices (GMP)" at its Swedish facilities. Among the 11 violations listed, the FDA cited that "there are no procedures for, nor documentation of, the ampoule inspection prior to any of the sterilization processes, and after the dry heat sterilization." Moreover, it cited a "failure to investigate, after a device has been released for distribution, any failure of that device or any of its components to meet performance specifications." As a result, the FDA banned Nobel's implants from importation into the U.S. According to industry insiders with whom we spoke, Nobel lost meaningful market share during the roughly six month ban.

In addition to lost sales, in a worst case scenario, we think that Nobel could also face a wave of lawsuits from practitioners, patients and investors. Following a recall, it would be convenient for a dental practitioner to attribute any past failures of Nobel implants to the package sterility issue, regardless of the actual cause of the failure. This could involve payment for failed product plus damages. Moreover, a Nobel recall could prove to be an attractive target for product liability lawyers. We note that attorneys have recently advertised for patients who have experienced problems with NobelDirect implants, which have had higher than average failure rates attributed both to poor implant technique and implant design.

In a worst case scenario, the FDA could institute a recall of all Nobel implants that have been shipped to date but not yet implanted in patients. In our opinion, this could prove very damaging to Nobel's business. As we previously discussed, we think the majority of practitioners would stop using Nobel products based solely on the potential liability. This could have a manifold negative impact on Nobel. First, it could be extremely costly to recover and repackage its entire store of inventory. Moreover, customers could be left without Nobel product for several months. According to our industry sources, Nobel does not yet have the packaging technology in place to rectify the situation. Furthermore, it would most likely have to conduct time consuming tests (accelerated time incubation tests) and attain certification before shipping new product, a process that could take 2-6 months, depending on its desired shelf life claims. Within that time period, competitors could approach Nobel customers throughout the world and offer to replace the "tainted" Nobel implants, perhaps using the opportunity to denigrate the company. Given the intense competitive environment, it is not difficult to envision a competitive assault resulting in the conversion of a meaningful amount of existing Nobel business.

The dental implant business has become largely marketing driven, with the top five companies spending lavishly on the sales and promotion of what has become an increasingly commoditized product offering. Based on our surveys, we think it is unlikely that Nobel would recapture a meaningful % of any lost market share. The damage to Nobel's reputation could also be significant especially if it is determined that management was aware of the problem and did not act quickly to rectify it. From the Nobel website: "Nobel Biocare is committed to ensuring that patients can trust its products for their reliability, quality, and superior performance...our own more stringent internal guidelines make patient health the top priority."