



## ***Comments to a Manuscript of an Unpublished Article on NobelDirect by Albrektsson et al.***

***(Submitted to SMPA 30 April 2007)***

### ***Executive summary***

The received manuscript is to a large extent a reiteration of known data. Out of the claimed 550 placed implants, 461 were already commented on by Nobel Biocare in a report to SMPA, dated August 31, 2006. In this analysis it was concluded that the data were incomplete and reported in an unscientific way.

The analysis of the present manuscript shows that the material still suffers from intransparency and lack of scientific stringency. The process for peer-review may even be questioned. This is in the light of the fact that one of the co-authors, Prof. Sennerby, is listed as one of two Editors in Chief for this journal.

Nobel Biocare can thus conclude that the scientific value of the presented manuscript is very limited. This especially in comparison to the 14 scientific references provided by Nobel Biocare. Four of these articles, including a two-year follow-up, have now been accepted for publication in peer-reviewed journals. Nobel Biocare refers in all respect to these articles and to all previous communication in support of the NobelDirect implant.

Based upon all available documentation, Nobel Biocare concludes that NobelDirect is safe and effective, provided the product is used according to instructions.

### ***Received material***

On April 16, 2007 Nobel Biocare received an unpublished article from SMPA “*Survival of NobelDirect Implants: An Analysis of 550 Consecutively Placed Implants at 18 different Clinical Centres*” authored by Albrektsson, Gottlow, Meirelles, Östman, Rocci and Sennerby, which was stated to be accepted for publication in Clin Impl Dent Rel Res.

A cover letter to Mr. Lennart Philipson at SMPA signed by Prof. Albrektsson was also received.

### ***Analysis of previously received data***

Already in the communication to SMPA, dated August 31, 2006, Nobel Biocare reviewed four unpublished manuscripts, including what seemed to be a summery report of available data; *Sennerby L., Preliminary results from a retrospective multi-centre study on the NobelDirect one-piece implant*. This report was based upon 461 implants placed in 12 centres. These implants are part of the now reported 550 implants. The Nobel Biocare

*Convenience translation  
of submission in Swedish*



analysis of these clinical data is shown below (page 15, Nobel Biocare communication to SMPA, August 31, 2006):

<i>Study Material</i>	<i>In total consecutive</i>	<i>Removed implants Failures</i>	<i>With claimed detailed information, i.e. jaw position</i>	<i>With information on jaw position, type of site and loading protocol</i>	<i>With x-ray measurements on bone level</i>	<i>With x-ray measurements on bone remodelling (pairs)</i>
<i># of implants</i>	461	33(7.2%)	331(72%)	326	250(54%)	220(48%)
<i># of patients</i>	?	?	134	<134?	?	?
<i># of centers</i>	12	8	10	10	?	?

- *Implants (461) consecutive, but the 250/220 implants with x-ray measurements are not stated consecutive as 167 (36% of total number of implants) implants remain to be examined. Average follow-up time 10.8 months (1-18 months). Thus, significant information is missing.*
- *33 implants have failed in 8 of the 12 centers. 17 with detailed information (52%); 13 removed due to extensive bone resorption, 3 were mobile and for 1 implant no reason for removal is stated. There is no information on number of patients.*
- *Radiography: methodology for reference material is not described, i.e. reference point/level.*
- *There is no claimed independent person/radiologist making the x-ray readings.*

*In the conclusion the 461 implants are stated as the basis. However, this is only valid for the failure rate. Any radiographic findings are based on 250/220 implants.*

In Prof. van Steenberghe's analysis it is stated (Nobel Biocare communication to SMPA, August 31, 2006, encl. 5):

*"It were 12 centers, but some have placed only 1 implant while 6 definitely placed less than 10 implants and are not what is normally meant by "centres". Indeed there is for every new item a learning curve. The centers are also not identified. From two centres (n° 3 and 4 in the manuscript) reporting 130 of the 461 consecutively placed implants (ND + NP), no data were available except for failure rate. The too limited number of implants placed in some location thus reduces this multicenter study from 12 to 4 relevant centers, where in total 134 patients have been treated and from 461 to 331 implants. The text says 163 were placed in the mandible and 168 in the maxilla but table 2 says the opposite."*

## **Analysis of present manuscript**

Nobel Biocare has forwarded the present manuscript to the following internationally recognized clinical experts:

Prof. Daniel van Steenberghe, Catholic University Leuven, Belgium

Prof. Asbjörn Jokstad, University of Toronto, Canada

Their comments are attached (encl 1 and 2).

### **1. Referenced literature**

- Ref (1) relates to a study on NobelPerfect, which is a conventional two-piece implant, i.e. it is irrelevant in this context.
- Contrary to standard practice, key references are not available to the reader. Access to ref (2) and ref (3) is needed in order to make a thorough analysis of the present manuscript. Prof. Jokstad states (encl 1):

*”it is not common amongst biomedical journal editors to accept references to papers that remain yet to be published, but I assume the editor of the Clinical Implant Dental Related Research has had his or her own reasons for doing so in this particular case”*

It should be noted that Prof. Sennerby is listed as one of the two Editors in Chief for this journal.

### **2. Analysis of data from participating centres**

- Contrary to normal practice, the participating clinical centres cannot be identified and the number of patients is not clearly defined. Furthermore, the number of participating operators cannot be identified. This is important information since the same operator may be placing implants in several centres. The lack of detailed information on patients and participating operators precludes a detailed analysis of cluster effects.
- The data from the 18 centres is skewed in that two centres represent 50% of the data, and 80 % were placed in only 4 centres. 7 centres have placed less than 10 implants. It is noticeable that centres contributing with 1 implant have been included. This is completely against common scientific practice and clearly diminishes the value of having multiple centres reporting in this material.
- For 80 implants, basic information on diameter is missing. This represents 14.5% of the material and 40.6 % of the losses (Table 3). It is remarkable that the basic information is not available for this group, which represents such

high amount of the failures. The absence of basic information would normally disqualify data from a participating centre.

### 3. Failure analysis

- It is stated on page 2 that “*failed implants are defined as those that have been removed from the jaws for one reason or another*”. Out of the 59 reported failures, the reason for failure was only analysed for one patient representing 3 implants. The reason for removal is not reported for the remaining 56 failed implants. This is against common scientific practice and is normally questioned by the editor of a peer-reviewed journal.

### 4. Authors' discussion

- The authors state, “*Table 1 presents seemingly different clinical outcome for different centres.* “ However, the authors have chosen not to provide a detailed analysis of this variation. One centre has reported 8 failures out of 10 implants while another centre reports 11 placed implants and no failures. As 1 centre with 1 placed implant that failed is included, the range of implant failure is 0 – 100% for the different centres.
- The authors state “*... that of 58 failures for immediately loaded implants (n=492) and only one failure (1.7%) if implants were placed with a surgical flap, and direct occlusion was avoided for some time (n=58)*”  
This statement is impossible for the reader to assess since details on the surgical procedures flap/flap-less is not reported in materials and methods.
- The conclusion made by the authors “*Therefore, the combined effect of recommended clinical handling procedures seems to be the most incriminating evidence for the observed problems with NobelDirect implant*”  
is completely lacking support in the presented data.

In the cover letter addressed to Mr. Philipson it is stated: “*förlustfrekvensen för de implantat som satts in med en kombination av stansprocedur, nedslipning in situ och direktbelastning är 11.8% vid en genomsnittlig uppföljningstid av ett år*”.

In the reviewed manuscript, information regarding surgical techniques and preparation of the implant is not reported for the entire material. Thus, the above statement is misleading and cannot be substantiated in the reviewed report.



## **Conclusion**

In the comments from both Prof. Jokstad and Prof. van Steenberghe the scientific stringency of this manuscript is questioned.

Prof. Jokstad states (encl.1):

*”Unfortunately, there is so much information left out of this paper that it is not possible to address the study validity”*

and Prof. van Steenberghe states (encl. 2):

*“The style of the paper clearly deviates from scientific traditions in Peer-reviewed journals because of the often-emotional tone. This normally does not favor the quest of truth. I would be surprised to hear that it has been properly referred.”*

*“For me the paper is clearly an editorial (or eventually an opinion paper) rather than a traditional scientific report as the title announces.”*

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