1 Summary

1.1 Appointment

On 18 January 2006, the Rikshospitalet–Radiumhospitalet Medical Center and the University of Oslo (UiO) jointly appointed a special commission to conduct an independent investigation in accordance with detailed terms of reference.

The background for the investigation was that a researcher employed by these institutions, Jon Sudbø, had admitted fabricating the raw data used for a scientific article published in the renowned medical journal *The Lancet* in October 2005.

1.2 The investigation

Early in the investigation it became clear that the entire body of Sudbø's scientific work from 1993-2006 (at least 38 publications) would have to be scrutinized, and that the co-authors (60 altogether) would in reality also have to be subject to investigation. All the authors received a letter requesting them to submit a voluntary written statement, which they all did. Moreover, information was gathered from relevant institutions and other relevant partners. Special mention should be made of the findings from the thorough investigations made by the Cancer Registry of Norway. The Commission also met with individuals and representatives of institutions, including Jon Sudbø. Furthermore, the Commission has obtained documents and other information from several other sources. Available data lists, etc., and published research results have been correlated and compared. Accordingly, the Commission was generally able to judge whether, and the extent to which, the underlying data on which the publications are based are genuine. As its main principle, the Commission has found it appropriate to apply a standard of evidence entailing a *qualified* preponderance of probability as a condition for accepting a particular fact as grounds for the report.

1.3 Findings

Jon Sudbø began his PhD project in 1993 under the supervision of Albrecht Reith.

The PhD project consists of two separate parts. One part involves theoretical and applied works on tissue architecture in cancerous tumors and normal tissue. The Commission has not found indications of research flaws related to these works.

As reflected in his subsequent research, most of his PhD project involved characterizing the early stages of oral cancer. The research question was whether and, if so, to what extent, different types of classifications of white patches in the oral cavity were indicative of a high risk for developing oral cancer. The doctoral dissertation and related publications give an affirmative response to this question, asserting that a classification based on DNA content can with great accuracy predict the subsequent development of cancer.

First published in the highly respected *New England Journal of Medicine* in 2001, this sensational finding was based on DNA analyses of 150 patients with leukoplakia (i.e. 'white patches' that may be early stages of oral cancer) in the oral cavity. In 2004, a second article was published in the *New England Journal of Medicine*, based on further investigations of the same 150 patients. Based on their own investigations and those made by the Cancer Registry of Norway, the Commission's point of departure is that there are serious problems associated with this crucial patient material. For instance, the same patient appears several times. As far as the Commission can determine, the material consists of 141 different patients at the most, since several patients are represented by several tissue samples that collectively add up to 150. Further, the Commission has found that 69 of the 141 patients included in the study should have been excluded because they had been diagnosed with oral cancer before or at the same time as the leukoplakia was diagnosed. For these patients, it was not possible to study the future development of cancer, since they already had cancer. This error alone is so serious that the results and the conclusions are invalid. The Commission has also uncovered several other inconsistencies. For example, the age distribution in the data files is not consistent with the underlying patient material. Further, the Commission has noted that the reported 150 DNA analyses are to some extent repetitions of data from a far smaller number of patients. The reporting on how DNA analyses and the classification of leukoplakia were conducted (by several observers) is also incorrect and misleading.

Consequently, the Commission has determined that the data underlying parts of the PhD project, as well as several other publications, are not sufficiently consistent with the actual facts the Commission has found it reasonable to take into account. The internal affairs investigation conducted by the Cancer Registry of Norway has arrived at the same conclusion.

The Commission is of the opinion that the errors and defects that have been exposed are too numerous, too great and too obvious to be attributed to random errors, incompetence or the like; and that the raw data therefore appear to have been fabricated, manipulated and adapted to the desired findings.

The consequence of this is that the doctoral dissertation and three related original articles must be retracted. In addition, subsequent publications must be retracted where they are based on the same raw material, as most of them are. On the same grounds, the Commission also questions one other original article. Further, the Commission has questioned an original article published in the *Journal of Clinical Oncology* 2005, *inter alia* in the light of circumstances partially acknowledged by Sudbø. The most recent original article published in *The Lancet* in 2005 has been retracted, since it is, in its entirety, based on fabricated raw data. Jon Sudbø has admitted this.

This means that the bulk of Jon Sudbø's scientific publications are invalid due to the fabrication and manipulation of the underlying data material.

1.4 Criticism, possible explanations and preventive measures

The exposed fabrication and manipulation of research data justify criticism against Jon Sudbø. The comments that Sudbø has made to the Commission in a meeting and after having read two draft reports with attached documentation, have not given the Commission reason to make any major changes in the preliminary conclusions drawn during the investigation.

In compliance with the terms of reference, the Commission has posed the question of how such – in retrospect – obvious and gross acts could have been perpetuated over such a long period of time in collaboration with so many well-qualified co-authors/scientists and research institutions.

The Commission points out that there will invariably be certain possibilities for a dishonest researcher to dupe and deceive others. Another factor is that Jon Sudbø has operated relatively independently both as a doctoral candidate and later as a researcher. He has always maintained full and sole control of the underlying data. In that connection, the Commission has found reason to criticize his supervisor for a lack of due diligence and academic supervision during Sudbø's fellowship. This case has also revealed what appears to be a systemic failure at the Norwegian Radium Hospital with respect to a lack of supervision, training and control procedures. Another circumstance is that there has been no formal permission or approval whatsoever of the project on the part of external bodies, nor has anyone taken it upon themselves to arrange for or check this. In this context, it has been noted that the institutions that contributed patient material have not required verification of the necessary permits, e.g. dispensation from mandatory confidentiality.

The Commission has not found indications that others, including some of the co-authors, have been involved in the fabrication and manipulation of research data or by other means been party to scientific misconduct. However, in good conscience and based on cost/benefit considerations, the Commission has not perceived its task as being to investigate less serious types of deviations from the norm. The co-authors can generally be divided into two groups: 1) suppliers (subcontractors), and 2) higher level guarantors (senior researchers), who to little or no degree contributed to or had knowledge of the underlying data material. Most communication has taken place through Jon Sudbø. Thus the co-authors have had little opportunity, as well as little reason, to check the underlying data and each other's contributions. Such a division of labour is not uncommon for medical publications that must necessarily be based on cooperation between researchers with rather dissimilar professional backgrounds and tasks, and thus require that they trust each other.

On the other hand, the Commission has pointed out certain factors to which several people should have reacted, be they co-authors, supervisors, superiors, opponents, colleagues or others. Since there have been a number of less serious mistakes on the part of several people that must be viewed in context (collective and cumulative mistakes), the

Commission has found reason to view this as systemic failure, where the responsibility rests with the institutions.

In light of this, the Commission has recommended that the institutions take more responsibility for raising awareness and instructing their researchers about the rules that apply, and that they engage in at least a minimum of verification and control, taking appropriate account of academic freedom.

The Commission has not perceived its task as being to expose specific damaging effects. This will probably be a topic for a subsequent investigation by the Norwegian Board of Health. Notwithstanding, the Commission has noted that colleagues, researchers, clinicians and individual patients have probably used Sudbø's research results, and it is therefore reasonable to assume that some of them have been affected. The serious implications of this must have been obvious to Jon Sudbø right from the start.

1.5 The Commission's Report – an overview

Chapter 2 of the investigative report presents the conditions of the Commission's appointment, the terms of reference and methods of working. The chapter discusses the investigative principle adopted, mode of information retrieval, the principle of contradiction, standards of evidence, the relationship to disclosure, and thresholds for criticism.

In Chapter 3, the Commission has found reason to outline the ethical and legal framework that applies to medical and health research. Here, the Commission provides a general review of the rules of authorship and supervision, etc.

Chapter 4 reviews the facts the Commission has chosen to take into account. The facts are presented in chronological order, beginning with Jon Sudbø's PhD project, which commenced in 1993. There is an explanation of the raw data underlying parts of Jon Sudbø's doctorate and several subsequent publications. The Commission discusses in detail which patient data Sudbø actually had or may have had, comparing it with the data Sudbø and his co-authors stated that they have had in different publications. The Commission then reviewed Sudbø's subsequent scientific publications, which are mainly based on the original raw data from the PhD project.

In Chapter 5, the Commission has attempted to illuminate certain circumstances that may help explain how and why things turned out the way they did.

Chapter 6 offers a brief discussion of the possible consequences of the situation, not least for Norwegian research and patients.

Chapter 7 summarizes the findings and the circumstances worthy of criticism which the Commission has found reason to point out. This criticism refers to individuals and institutions alike.

Finally, the Commission has made certain recommendations in Chapter 8 by way of conclusion.