Report from the Investigation Commission

appointed by

Rikshospitalet – Radiumhospitalet MC and

the University of Oslo January 18, 2006

Submitted June 30, 2006
To Rikshospitalet – Radiumhospitalet MC and the University of Oslo

The investigation committee appointed on 18 January 2006 hereby submits its report.

The report is unanimous.

Oslo, June 30, 2006

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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 coauthors (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 proof based on 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,
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 coauthors/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 coauthors, 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 proof, 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.
2 The Commission’s appointment, terms of reference and method of work

2.1 Appointment of the investigation Commission
On Friday January 13, 2006, the Rikshospitalet-Radiumhospitalet Medical Centre (RR MC) and the University of Oslo informed media that a scientist employed there had admitted to fabrication of data underlying a scientific article in the renowned medical journal The Lancet.

On Wednesday January 18, 2006, the Rikshospitalet-Radiumhospitalet MC and the University of Oslo made it known that they would appoint a special Commission with detailed terms of reference (section 2.3) to perform the investigation and clarify the facts.

2.2 The Commission’s composition
The Commission was composed as follows:

- Professor Anders Ekbom, M.D., (Chair), Institusjonen för medisin, Karolinska Universitetet Sjukhuset, Stockholm
- Special Advisor Gro E.M. Helgesen, Cand.Pharm., the Research Council of Norway
- Post doc Tore Lunde, LL.D, the Faculty of law, the University of Bergen
- Researcher Aage Tverdal, Professor, PhD., the Norwegian Institute of Public Health
- Professor Stein Emil Vollset, PhD, the Department of Public Health and Primary Health Care, the University of Bergen

- Research fellow Sigmund Simonsen (Secretary), Master of law (Norway), LL.M, the Department of Community Medicine and General Practice, the Norwegian University of Science and Technology.

In addition, the National Cancer Institute (NCI), USA, was offered a seat on the Commission, but has not accepted the invitation.

2.3 The Commission’s terms of reference
The purpose of the investigation is to identify and review all factual matters in connection with the research article “Non-steroidal anti-inflammatory drugs and the risk of oral cancer: a nested case-control study” by J. Sudbø et al. in The Lancet, vol 333, pp. 1359-1366, October 15, 2005. The Commission shall also assess other research and other matters considered by the Commission to be related to this case.
The Commission shall make such investigations as it finds necessary to clarify the extent of the breach of standards of scientific research and other criticizable factors.

The Commission shall attempt to clarify whether there are special factors that have influenced what has been done in this case, including the researchers’ self interests as well as whether special external interests, frameworks, conditions and tying arrangements for the activity exist.

The Commission shall map and assess any harmful consequences of the research and of other factors included in the terms of reference. This applies to whether this has been harmful in connection with the treatment of patients and if so what harmful effects have ensued. The Commission shall also attempt to map and assess the negative effects caused to the scientific research at the Rikshospitalet-Radiumhospitalet MC and relevant areas of research at the University of Oslo as well as scientific research at other institutions.

The Commission shall assess rules and routines for control and quality assurance which apply to scientific research at the Rikshospitalet-Radiumhospitalet MC and the University of Oslo, and whether these have been complied with in this case. The Commission shall assess whether these rules and routines should be changed, and if so, submit proposals for such changes.

If the Commission during its work should become aware of factors that have effects which should be notified prior to the conclusion of the Commission’s work, the Commission must bring this to the attention of the appointing institutions as quickly as possible.

Should the Commission be of the opinion that the terms for reference are limiting the work, this must be brought up with the appointing institutions immediately.

The Commission shall submit its report to the Rikshospitalet-Radiumhospitalet MC and the University of Oslo no later that April 1, 2006, whereupon the report will be made public at the same time as being dealt with independently by the Boards of the two institutions.

2.4 The legal status of the Commission, legal framework, procedural rules, and principles for the investigative process

2.4.1 The Commission’s legal status

The investigation commission was appointed by the Rikshospitalet-Radiumhospitalet MC (RR MC) and the University of Oslo (UiO) (hereinafter the “Appointing Institutions”) which are, or have been, the employer of the researcher who has admitted to having fabricated research data, and who was the cause of the investigation. This means that the Appointing Institutions are two public institutions.
The Commission is not a “public investigation commission”, but rather a temporary and professionally independent administrative body of a special nature, comprised by unbiased experts, created by the management of the aforementioned two public institutions jointly for this case to perform an investigation on their behalf. A fundamental consideration for the Appointing Institutions as well as the Commission has been to have a professionally independent investigation.

There are no particular procedural rules laid down in statute or regulations for this type of ad hoc appointed commissions. In 1968, a committee appointed by the Government submitted a Recommendation for Rules for Investigation Commissions (printed in 1969). The Ministry of Justice then prepared a circular\(^1\) containing a mixture of information, instructions, guidelines, and provisions of a more mandatory nature\(^2\). The circular is aimed at public investigation commissions appointed by the Government or a ministry, so-called “public investigation commissions”. It is therefore obvious that these guidelines are neither prepared with this Commission in mind nor binding for it.

Since the Commission is a body for two public bodies, it is clear, however, that the Commission is subject to the Public Administration Act and general non-statutory requirements as to generally accepted administrative practice. Since the Commission’s report is not an individual decision in the terms of the Public Administration Act, only chapters II and III of the Public Administration Act have been of particular importance to the work.

2.4.2 Impartiality and independence

In accordance with the provisions of section 8 of the Public Administration Act, the Commission has considered its own impartiality. No committee member is related to the parties to the case, and the Commission cannot see that circumstances exist that are apt to impair confidence in its impartiality, cf section 6 of the Public Administration Act.

The Commission has placed great emphasis on the consideration of independency in the contact between the Commission and the Appointing Institutions. The Appointing Institutions have made conditions favorable so that is has been possible to carry out the investigation independently, self-contained and without restrictions on the use of resources. Out of consideration for the Commission’s independency, its secretariat has not been physically or functionally localized together with the Appointing Institutions, persons or institutions that could have become the subject of investigation. Thus the Commission has made use of premises for the secretariat in Trondheim, and most of the meetings have been held in meeting rooms at Gardermoen [Oslo Airport] in addition to telephone meetings. One meeting was held at the Radiumhospitalet in connection with an inspection and talks with employees, and one meeting was held at the Cancer Registry. The Commission has had good framework conditions for carrying out the investigation.

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\(^1\) Rundskriv G-48/75 of March 4, 1975 "Regler for granskningskommissjoner"
\(^2\) Bratholm A. Granskninng som statlig virkemiddel for å bringe faktiske forhold eller ansvarsforhold på rene [Investigation as a governmental tool to bring actual facts or responsibility relationships to light]. Lov og Rett, 1986: p. 439
2.4.3 **Legal measures**

The Commission is not authorized to make searches or seizures. People to be interviewed were not under a duty to give any statement to the Commission. The legal basis for obtaining evidence, in the form of oral and written information, including emails and interviews, is consent. All the persons the Commission wanted to interview consented in providing information to the Commission. The same applies to other persons and institutions to which the Commission has addressed inquiries and questions. In general, persons and institutions concerned have collaborated well with the Commission. Nobody refused to collaborate with the Commission.

2.4.4 **The duty to clarify the case principle and the sound procedure principle**

The Commission has observed the duty to clarify the case principle in section 17 of the Public Administration Act and the principles inherent in requirements as to sound procedure and generally accepted administrative practice. Within the limited time frame available, the Commission has sought to obtain the widest possible information basis, which has included making critical checks of information received from various sources and comparing these against each other with the aim of discovering any discrepancies.

However, the Commission points to the difficulties caused by the fact that some of the circumstances subject to investigation occurred more than ten years ago. Such a comparatively long time span obviously influences the interviewed persons’ possibilities to recall details of what took place. The reservations which for these reasons have been necessary to make in relation to what can be deducted from the evidential material, have nevertheless not altered the Commission’s main conclusions, as these are stated in the report.

2.4.5 **Contradiction**

In order to ensure a reliable procedure in line with fundamental considerations of the due process of law and requirements as to generally accepted administrative practice, the Commission has taken as its point of departure, and practiced, the guiding norms laid down in the circular as far as serviceable and natural. The individuals who have been investigated have been notified of this and they have been urged to contribute voluntarily. At the same time, they were informed that they might be subject to criticism and that they in such a case would be notified especially if this would be the case. The individuals who are subject to criticism have also been allowed to read memos, documents and finally the draft report itself, i.e. Chapter 4 through Chapter 7 (Chapters 1 through 3 and 8 contain more general considerations). Thus they have been given the opportunity to respond to the criticism and make contributions at several occasions. The Commission has also met with these persons.
The Commission will here note that the most central person in the investigation, Jon Sudbø, was assisted by his lawyer during the investigation. The procedure and factual matters have been discussed with Sudbø and his lawyer throughout. No substantial objections to the Commission’s outlined plan for the investigation as such have been made. In this context the Commission notes that Sudbø’s office material has been locked away by his employer during the entire investigation and that Sudbø has been given several offers of access to this material in order to extract documentation and the like of importance to this case. Sudbø has been sent two draft reports together with data lists, connections and other key documents on which the Commission has based itself. Sudbø submitted detailed comments to the first draft – which the Commission incorporated, but did not want to comment on the next draft he received.

In other words, the Commission has arranged for contradiction to a larger extent than it was obligated to do. This was done in consideration of individuals affected, but also in order to illuminate the case as well as possible.

2.4.6 Requirements of proof and thresholds for criticism

The Commission’s primary task is to clarify the facts with the aim of discovering whether and to what extent breaches of standards for scientific research and other blameworthy acts have occurred. Like in legal procedures – both civil procedure and criminal procedure – also in investigation procedures there will be different degrees of proof for establishing facts as probable. The Commission has considered what degree of proof should be required in a case of this nature in order for the Commission to rely on particular facts as a basis for criticism.

In the Commission’s opinion there are several reasons why a more stringent degree of proof should apply than the traditional principle in civil procedure of proof by a so-called simple preponderance of probability. In the first place reference is made to the fact that the object of the investigation is to clarify facts with the intention of discovering the extent of scientific dishonesty and the like. Criticism on such a basis must be considered highly invasive for the individuals involved. Taking into account the serious legal consequences and any sanctions that may be triggered by conclusions that scientific dishonesty, breach of generally accepted research practice and similar criteria exists, the ordinary principle of proof by a preponderance of probability must be deviated from in favor of the person concerned by the investigation. In the second place, in an investigation process the production of evidence and practice of the principle of immediacy will be more limited than during an ordinary court procedure. On the other hand, the Commission finds that there is no basis for requiring a degree of proof that is as strict as in criminal law. Based on an overall assessment, the Commission finds that the degree of proof to be applied in order for it to rely on a particular fact as proven should be proof by a so-called qualified preponderance of probability. The Commission has applied this principle in its investigation and preparation of the report.

The Commission has therefore, mainly out of regard for the due process of law, but also for pragmatic reasons, applied a very high threshold for criticism of persons. Many individuals have been involved in the research which has been subject to investigation, and, in the Commission’s view, any criticism for less serious acts may have a disproportionate effect on individuals, especially seen in the light of the Appointing Institutions’ express intention to publish the report as well as the extensive press coverage this case has been the subject of.

In relation to the institutions involved, however, the Commission has found grounds for a somewhat different approach. The Commission has notified two institutions that they might be subject to criticism. These institutions have been given the opportunity to read the criticism itself, but not the draft report in its entirety, and have thus been given a limited possibility to contribute. Furthermore, the Commission has chosen not to notify the Appointing Institutions: the Rikshospitalet-Radiumhospitalet MC and the University of Oslo, although these as responsible institutions must suffer criticism. Notification has been omitted to prevent the risk of any unfortunate influence from these institutions. However, the Commission has had meetings with managers at several levels at the Rikshospitalet-Radiumhospitalet MC and the University of Oslo in order to clarify factual matters. The omitted notification and possibility to read the draft report are also related to the institutions’ relative strength compared to individuals. The consideration for the Commission’s integrity and professional independency has also been an important element in this assessment. The Commission has considered it such that the institutions to a completely different degree than individuals must put up with public criticism.

2.4.7 The presumption of innocence

The so-called presumption of innocence embodied in the European Convention on Human Rights (EHRC) Article 6 (2) states that “everyone charged with a criminal offence shall be presumed innocent until proved guilty according to law”. The Convention has been incorporated into Norwegian law, cf the Human Rights Act. The Commission’s terms of reference have been established with the aim of clarifying factual matters particularly related to the Lancet article, and discovering the extent of breach of standards for scientific practice. The formulation of the terms of reference implies that the Commission may perform its tasks without making findings of guilt that violate the presumption of innocence.

2.4.8 Publicity

The Commission is an administrative body in the terms of section 1 of the Freedom of Information Act. The Freedom of Information Act thus applies to the Commission’s work. All documents
supplied to the Commission are subject to disclosure unless the grounds for exemption in sections 4, 5, 5a or 6 apply. Recording of statements, draft reports and similar notes are considered internal documents which may be exempted pursuant to section 5. This also applies to contributions and support documents supplied to the Commission by persons who have given statements, as well as in-depth comments they have given to print-outs sent them for perusal. Voluntary public access has not been given to statements recorded during the investigation. The Commission has received one request for access to documents, by Verdens Gang [a major Norwegian daily newspaper]. The request was refused pursuant to section 4 (1) of the Freedom of Information Act. Following a complaint from Verdens Gang and a renewed assessment, certain documents were released.

When preparing the report, the Commission has had in mind the Appointing Institutions’ express aim to make the report available to the public. Annexes that document errors and defects in the patient material and that contain patient-identifiable information (in the form of block numbers, for example) have been exempted from disclosure and have only been submitted to the Appointing Institutions and the persons and institutions against which the criticism has been directed and which in that capacity previously have been dealing with these data. An anonymized and simplified version of these annexes, without patient-identifiable information, has been included as an annex to the report which will be published.

The Commission will be dissolved after the submission of the report to the Rikshospitalet-Radiumhospitalet MC and the University of Oslo, and the documents in the case will then be handed over to and managed by the Rikshospitalet-Radiumhospitalet MC and the University of Oslo for filing in the normal manner. The material will be subject to the Freedom of Information Act and the legislation on archives. Any subsequent right of access may, moreover, be limited due to restrictions which may follow from consents given, secrecy rules and the like.

2.5 The Commission’s relation to the terms of reference

The terms of reference are stipulated very broadly. The formulation of the terms of reference must be seen in the light of the fact that the Appointing Institutions at the time of appointment obviously did not have a full view of the more detailed nature of the case and its extent, and that one did not want to place restrictions on the Commission’s investigation.

Furthermore, the Commission has noted the extensive press coverage and debate which followed in the wake of this case, including more or less explicit expectations to the Commission held by commentators and others. Obviously, the Commission has neither tried nor had any possibility to accommodate all such expectations.

However, in line with its terms of reference, the Commission started out broadly and considered a series of relevant factors. At the same time it was evident that it would have been an insurmountable task to make an equally thorough assessment of all the questions raised in the terms of reference within the limited time frame at the Commission’s disposal. The Commission has therefore had to make continuous
delimitations and definitions of the terms of reference. The Commission has then had to prioritize those factors that in the Commission’s view have appeared as the most central and serious.

In the terms of reference the Commission was asked to submit its report to the Appointing Institutions no later than April 1, 2006. The Commission gradually saw that it would not be possible to comply with this deadline. A new deadline was fixed at June 30, 2006 according to the Commission’s own suggestion.

2.6 In more detail about the Commission’s method of working

2.6.1 In general

The members of the Commission have performed their assignment in addition to other tasks. The Commission’s secretary has worked full time for the Commission and also had a 20% position at the NTNU. Furthermore, the Commission has received assistance with office work, i.a. for transcription of interviews, from Marit Kvidal and Toril Synnøve Strand. All have signed a statement on confidentiality.

2.6.2 Meeting activity

The Commission has held 13 all day meetings and 11 telephone meetings. A fair amount of the meeting time has been spent to meet key persons – altogether 15.

2.6.3 Retrieval of information

The Commission’s principal task has been to clarify the facts. The Commission has obtained written as well as oral information. The scope of information is considerable. The written material is stated in document lists included as annexes to the report. The material can be grouped into 1) research publications in which Jon Sudbø was the first author or coauthor, 2) correspondence, including email between the Commission and persons, institutions and public authorities involved, and 3) data files containing information on background material used, including data files prepared by the Commission with the aim of reconstructing and checking the background material. All information has partly been recorded on tape and then transcribed, partly received per telephone and recorded in internal case documents and/or exchanged per email to the members of the Commission, and partly received in meetings, without tape recordings having been made, but where information has been recorded in internal case documents. The Commission has used information relevant to the terms of reference only.

It is inherent in the terms of reference that it is research under the auspices of Jon Sudbø that has been at the centre of the work, because Jon Sudbø, based on the information existing as per the time of the
appointment, already had admitted to fabricating research data as regards an article in The Lancet from October 2005.

Consequently, the Commission decided early on, in view of the nature of the case, that the entire scientific activity and production by Jon Sudbø, which according to the data base PubMed\(^4\) comprise 38 publications, had to be investigated, see the publication list, Annex 1. A more detailed account of this is given in the review of the facts in Chapter 4.

This meant that the authors who had contributed to publications together with Jon Sudbø (approximately 60) in fact also have been subject to investigation. These persons have been treated equally. The authors were notified in writing that formally they were subject to investigation, and formally notified that this could result in criticism. At the same time, they were asked to make a written statement voluntarily. They were also informed that they were under no duty to give such a statement, since the Commission had no authority to order statements from anyone. The authors all responded to the Commission’s request. In addition, certain persons and collaborators who are thanked in Acknowledgements were contacted. The Commission has also asked additional and follow-up questions as needed. Several authors and collaborators have also given oral statements before the Commission (15 persons). Jon Sudbø has made oral and written statements to the Commission. With the understanding of the persons interviewed, most of the statements have been recorded on tape and transcribed. Those who have given statements have been given the opportunity to read the transcripts from the conversations, and submit corrections, definitions or additional comments. In accordance with the conditions for tape recording stipulated by the interviewed persons themselves, the tapes have been deleted by the Commission.

The Commission has also obtained written and oral information from relevant bodies and institutions with which Jon Sudbø has been in contact in connection with his research. Particular mention should be made of the Cancer Registry of Norway, which itself has performed very extensive investigations as part of its own internal control, i.a. because the Cancer Registry allegedly has been a key cooperation partner for Jon Sudbø. The Cancer Registry’s independent investigations have been of great value to the Commission, first and foremost because the Cancer Registry has access to most of the background data used by Sudbø in his research.

As accounted for in detail in Chapter 4, the key information carrier has been available data lists and published research results which could illuminate the background material which forms the basis for Jon Sudbø’s research. These data files have then been correlated and compared with each other and other available documentation, i.a. from the Cancer Registry. In this way, the Commission has tried to

\(^4\) www.pubmed.gov
recreate the actual background material which has or with a high degree of probability has been used by Jon Sudbø in his research.

2.6.4 Good scientific practice, norm deviation and dishonesty

As already stated, one object of the investigation has been, through a clarification of the facts, to discover whether any breach of good scientific practice, i.e. breach of good research practice, has occurred. The Commission has subsequently delimited this object to apply to gross and serious breaches. This means first and foremost “scientific dishonesty”, as this has been defined traditionally, as well as more serious degrees of negligence and blameworthiness. The criterion “scientific dishonesty” has recently been enacted in the Act on Research Ethics (not yet in force) in which section 5 (2) reads:

“Scientific dishonesty means falsification, fabrication, plagiarism and other serious breaches of good scientific practice perpetrated with intent or gross negligence in the planning, implementation or reporting of research.”

In view of the fact that the requirement of guilt for scientific dishonesty is formulated as a requirement of intent or gross negligence, the Commission has applied a relatively high threshold for finding breaches of scientific honesty, as well as gross and serious breaches of good research practice. The Commission also refers to section 3.2. On this basis, the Commission has not considered it appropriate to make a detailed investigation of each one of the 60 authors, with the aim to discover deviation from norms which must be considered to be of less importance in relation to the main issue in this case.

This important delimitation is first and foremost justified by the fact that such less serious cases are in an entirely different category from the serious allegations which it has been the Commission’s primary task to investigate. It should be underlined that this must not in any way be construed as an attempt by the Commission to play down petty offences. On the contrary, the prevention of any form of norm deviation from good research practice has been given great emphasis in the Commission’s recommendations. The delimitation must rather be seen in light of a real and everyday need to establish a practicable framework for the Commission’s work. Within the Commission’s restricted time frame it has not been possible to investigate each individual author in detail, with the requirements as to thoroughness and due process this would have entailed. The Commission here refers to the fact that each individual person who the Commission might have found reason to criticize directly, regardless of whether trivial or serious acts were involved, would have had to be given the opportunity to give a statement and refute any criticism directed at him/her (the contradiction principle). Finally, the Commission emphasizes that the work connected to
discovering the most grave and serious acts has been much more extensive than what one had reason to predict in the beginning.

On the other hand, the Commission has found reason to present certain more general remarks related to how researchers and research institutions should act, including the lesser norm deviations which seem to have occurred. Thus, the criticism of persons is first and foremost related to gross and serious norm deviations, whereas the detection of less serious matters has been restricted to a more general and institutional level.

Accordingly, two questions have been at the centre of the Commission’s clarification of the facts:

1. Have gross and serious breaches of good research practice taken place, and if so, to what extent?
2. What happened (causal factors), and who is responsible for any breaches of good research practice?

Before replying to these questions, the Commission has found reason to outline the general framework and the background against which this specific case has been assessed, see Chapter 3.
3. Regulation of medical research

3.1 Overview of the applicable set of rules

The second section of the terms of reference reads:

“The Commission is to make such investigations as it finds necessary to clarify the extent of breaches of standards for scientific research and other blameworthy matters.”

“Breaches of standards for scientific research and other blameworthy matters” is a very broad concept. The concept aims at acts and omissions which are in breach of established norms of operation/rules of operation – here: good research practice. Such norms or rules for accepted conduct may have different status and designation, as for example:

- Ethical norms and social norms
- Vocational norms (researchers and medical staff’s self regulations)
- Instructions and norms laid down by the employer
- Legal norms (statutory and non-statutory legal rules)

The regulation of medical and health related research is marked by an intimate interaction between ethics, law and the profession’s own norms, where the ethics (ethical reflections) normally forms the basis for legal norms as well as the profession’s own norms.

The Commission will not here give a detailed description of all relevant rules that apply to medical research. These rules have recently been described comprehensively in other presentations, and the Commission would refer to these. However, the Commission will very briefly outline the existing legal framework against which this specific case has been assessed. The framework defines the expectations and requirements made to Norwegian researchers and research environments.

Although, basically, research is to be free and independent, there are of course rules of the game which researchers must follow in the same manner as everybody else.

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5 See for example Ruyter KW. Forskningsetikk [Research Ethics]. Oslo: Gyldendal, 2003
6 See for example Benestad HB, Laake P. Forskningsmetode i medisin og biofag [Research method in medicine and bio subjects] Oslo: Gyldendal, 2004
7 See for example Simonsen S, Nylenna M. Helseforskningsrett [Health Research Law] Oslo: Gyldendal, 2005
There are a series of rules and control routines for medical and health related research. Traditionally, the research community has regulated itself, via the development of norms for good scientific practice (professional norms and sector practice). In later years however, the legislative authorities have also played a more active role, particularly as regards medical and health related research that involves people, human biological material and/or personal data.

The Patients’ Rights Act, the Biobanks Act and the Personal Data Act are key examples of statutory legal rules. Non-statutory legal rules come in addition. A series of written and unwritten professional norms (self regulations), as for example the Helsinki declaration prepared by the World Medical Association (WMA) and the so-called Vancouver rules, cf section 3.5, are moreover still highly relevant. More detailed working instructions or implied requirements as to acceptable conduct at the individual research institutions come in addition. These are currently available at the institutions’ intranet. An increasing amount of international directives and conventions are also influencing the regulation of medical and health related research, and contributes, i.a., to many similarities between the national regulations in various countries. The EU Personal Data Directive 1995 and the Medicine Directive 2001, as well as the European Council’s Convention on Biomedicine and Human Rights 1997, are examples of the latter.

A public committee which reported on the regulation of medical research, the Nylenna Committee, found that a lack of regulations was not the primary problem, although certain flaws existed. In the committee’s view, the main problem was that the regulations were fragmented, complex and inaccessible, and that very few people for that reason seemed to have satisfactory overview of the set of rules. In order to obtain an overview of the current set of rules for research, it may be appropriate to differentiate between various types of norms of operation for medical and health related research, based on the purpose of the norms (although these obviously must be seen in connection):

- **Protective rules**: These concern rules aiming at protecting the integrity of the individual person (research participant).

  The main rules are that consent by the individual research participant (i.e. the person participating in the research directly or indirectly, i.a. by giving tissue samples or personal data) must exist. In addition, the research must be sound and in line with good research practice, as well as be assessed in advance by one of the regional committees for Medical Research Ethics (REK) and other relevant bodies.

  The regulations do not only comprise research on humans, but also the use of exclusively human biological material and personal data. Violation of these rules will often be considered as serious.

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because they jeopardize other people’s life and health, or infringe their integrity (private life). These regulations are therefore often a result of statutory provisions or non-statutory law.\textsuperscript{10}

The Human Rights Act 1999, the Medical Personnel Act 1999, the Patients’ Rights Act 1999, the Specialist Health Services Act 1999, the Biobanks Act 2001, the Personal Data Act 2000 and the Personal Health Data Filing System Act 2001 are key statutes in this field. The so-called Helsinki Declaration 1964\textsuperscript{11} indicates principal professional norms. The legislation relating to the protection of animals comes in addition in the case of experiments on animals.

- **Rules for scientific integrity**: This concerns rules aiming at regulating the research itself, as for example norms for the choice of method, design of studies and the like, which are to ensure that research results are valid and that the knowledge can be generalized. It is therefore fundamental that data should not be manipulated, fabricated or falsified. Furthermore, the inclusion of research participants must not be unduly selective, and research data must be stored for some time after completion in order to secure the opportunity to check. Honesty, thoroughness, completeness and openness are key ideals here.\textsuperscript{12}

  Violation of one or several of such norms of conduct/rules (good scientific practice) may entail that the research results cannot be considered as valid.

  These rules are primarily unwritten and follow from established scientific practice and good research practice as well as more general requirements to soundness.

- **Publication rules (integrity rules)**: A third group of regulations are those applying to the publication of research results. This concerns rules that are to contribute to openness around and opportunity to check research results, i.e. that what is written in the publication is in fact correct and adequate, such that others can use it as a basis for their further work. That which speaks for and against (positive as well as negative) results must be stated. Conflicts of interest, associations and the like which can be imagined to have influenced the results, should also be stated. Another dimension,


which can also be said to belong in this “group of rules”, is rules and practice concerning authorship, plagiarism and copyright.\textsuperscript{13}

These rules also primarily follow from established scientific practice and good research practice, as well as more general requirements as to soundness. The Copyright Act 1961 and the so-called Vancouver rules may also be relevant in this context.

\subsection*{3.2 Different degrees of norm deviation, guilt and blameworthiness}

It is important to emphasize that deviations from norms and breach of rules occur in many shades – from the trivial to the conspicuous.\textsuperscript{14}

In the recently enacted Research Ethics Act (not yet in force) section 5 (2), the so-called \textit{scientific dishonesty} is restricted to certain gross and serious deviations, i.e. “falsification, fabrication, plagiarism and other serious breaches of good scientific practice perpetrated with intent or gross negligence”.

Obviously also “less serious” deviations occur, which may nevertheless represent a breach of good research practice, as for example flawed source references, failing design, breach of quality assurance routines, misleading authorship, or by “disregarding” extreme or unexpected observations and other oddnesses which do not entirely agree with one’s own hypotheses. Such deviations must also be taken seriously, since they are suited to impair the quality and trustworthiness of the research, and to create a climate for more serious deviations.

Thus there is a sliding transition from the trivial to the gross and more serious deviations.

In the same way, the degree of guilt will vary, from excusable mistakes via cases in which one has acted unintentionally but nevertheless should have acted differently (negligence), to willful breach of the rules, knowingly committed. Norm deviations may thus be criticizable and blameworthy even if the researcher has not acted knowingly, but maybe rather been negligent, uninterested, careless, incompetent or the like.

The degree of blameworthiness will thus depend on the degree of the norm deviation and guilt.


3.3  **Personal liability and overall system responsibility**

The main rule in Norwegian law is that an individual is liable for his/her acts and omissions. Thus the individual person may be held personally liable for what he/she has done, alternatively not done, but ought to have done, and be met by different sanctions. This follows from general principles of non-statutory negligence liability and more special liability rules, among other things.

The large majority of researchers, however, are ordinary employees in public or private sector. This means that in addition, it may be question of a system liability for the employee’s superior, i.e. the person/organisation who is liable for the person who actually performs the act. Personal liability does not exclude system liability, and vice versa.

Basically, employers are liable for the acts of their researchers, and the main rule is that they are liable for the acts of their employees, irrespective of whether the employer is to blame or not. This so-called employer liability follows from section 2-1 of the Act relating to Compensation for Claims, of which subsection 1, first sentence, reads:

> An employer is liable for damage caused willfully or negligently during the employee’s performance of work or assignments for the employer, taking into account whether the expectations the parties sustaining the loss reasonably can make to the activity or service have been neglected.

For example, research is stated as one of the main tasks of the specialist health service on the same level as medical treatment, cf section 3-8 no 3 of the Specialist Health Services Act. The requirements in the Specialist Health Services Act relating to soundness, organization and management at different levels will thus apply to research. The medical centers have a hierarchic system, with the state as owner, having in principle the superior responsibility as well as the managerial prerogative and right to instruct, cf sections 3 and 7 of the Health Enterprises Act. However, the state has appointed a board of directors, which again has appointed a general manager, a CEO, having the day-to-day responsibility and managerial prerogative and right to instruct, cf section 37 of the Health Enterprises Act. But this responsibility, including the managerial prerogative and right to instruct, will be delegated downwards and distributed to clinical managers, department managers, sections heads and project managers (including project managers for research projects, i.e. the person having the day-to-day responsibility for a specific research project). Section 3-9 of the Specialist Health Services Act states that there shall be a responsible manager at each level. But such hierarchic delegation (line management) does not mean that the superior person in the line ceases to be liable. In principle, nothing prevents the overall liability to be divided, for example between a medical centre and a

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15 Buskop T. Hvem har ansvaret for et forskningsprosjekt? [Who is responsible for a research project?] www.forskningsjus.no. 2006.

16 Simonsen S, Nylenna M. Helseforskningsrett [Health Research Law] Oslo: Gyldendal, 2005
university. In such cases, however, it will normally be a question of joint and several liability, i.e. that both institutions are liable irrespective of each other – one for all, all for one. In general it must be assumed that the institution to which the day-to-day research has its closest relation, typically the hospital, carries the primary responsibility for the research.

Preparation and sound organization of the research, stating responsibilities and such like, are thus key tasks for the employer, i.e. the research institution. Where research is concerned, proper account must of course be taken of the customary academic freedom, i.e. that the employer must not in any undue manner try to influence the research. The employer may nevertheless not provide employed researchers with unlimited authority and disclaim any liability. Thus the employer may also be held liable on an independent basis, for example due to lack of routines, training, management, control and supervision in connection with research as well as medical treatment. This applies in particular when patients, patient material, patient data, animals or other sensitive research objects are involved in the research.

The current Act relating to Universities and Colleges of April 1, 2005, states explicitly in section 1-5 that universities and colleges may not be instructed regarding the academic contents of their teaching and the content of research or artistic or scientific development work. In evaluations of Norwegian research a stronger professional management is at the same time called for. Professional management and management structures may establish frameworks for research to be performed by the individual employed scientist. Tension may therefore exist between the individual person’s academic freedom and the institution’s professional management responsibility at all levels, even if the act does not contain provisions that directly can be said to restrict the individual academic freedom in an unfortunate way.

The recommendation, Innst.O. nr 70 (2005-2006), from the parliamentary standing committee on church, education and research concerning the Act on Research Ethics, states:

The committee takes as its point of departure, as did the Government, that research takes place under a considerable degree of freedom and trust, and thereby also a considerable degree of personal responsibility for the individual researcher. At the same time, there is reason to underline that the research institutions have an independent responsibility for control and management. However, the institution’s professional management responsibility must continuously be assessed against the concern for academic freedom and the individual scientific employee’s rights. The committee has noted that this issue will be discussed by the so-called Underdal committee, which is to submit its recommendation in October 2006.

It should be noted here that employed researchers, in spite of these formal points of departure, traditionally have had an extremely free role at most of the public research institutions, among other things indeed to secure the professional independency of research. However, it should be noted that there is not necessarily a contrariety between professional integrity and independency, and an overall responsibility for and supervision of the institution’s activity being sound.
A need to raise awareness of the research institutions’ responsibilities and duties is a common subject in reports on the regulation of medical and health research.17

Supervisors in PhD or master degree projects may have different roles, and do not necessarily form part of research institutions’ line management. In clinical research, the supervisor will often also be a co-researcher, and then usually a project manager, so that this person holds the day-to-day responsibility for the specific research project. The supervisor will then have an overall line responsibility for the PhD candidate or the student. But the supervisor may also have a more retired role by functioning solely as an advisor and conversation partner (mentor). In such cases, the supervisor’s responsibility will be more modest and derivative. The role as supervisor is discussed in more detail in section 3.7.

3.4 The application of the rules in time

A basic principle of the due process of law is that the rules prevailing at the time when the act of omission occurred shall apply.

Because circumstances in this specific case span a period from 1993 to 2006, it has been important to the Commission to clarify the rules in force at all times.

As a point of departure, one may say that the current main principles, as presented above, have been unchanged since 1993 when John Sudbø started his PhD project and his scientific career. Scientific dishonesty was, in other words, as unacceptable then as now.

In this connection, the Commission has obtained statements from the Regional Committee for Medical Research Ethics-South, the Data Inspectorate, the Norwegian Social Science Data Services and the Directorate for Health and Social Affairs. These bodies clearly state that the current rules in the areas that have been relevant in this case in all essentials correspond to the rules and principles existing and being practiced in 1993. As an example, the requirements as to a licence for, and an advance assessment of, research projects by the Data Inspectorate and the Regional Committee for Medical Research Ethics respectively applied then as now. The same was true for the requirement for either a participant consent or dispensation from the duties of secrecy by the Directorate for Health and Social Affairs for the use of patient information in research subject to a duty of secrecy. Earlier, prior to January 1, 2002, this public authority task was vested in the Norwegian Board of Health.

On the other hand, a certain tightening of the rules at the more detailed level, as for example the rules on the protection of personal data, has taken place. The most important is perhaps an increasingly raised awareness surrounding the rules that apply among researchers, institutions and public bodies.

The employees at the Rikshospitalet-Radiumhospitalet MC and the University of Oslo have also been given increasingly more and more defined internal rules and instructions to relate to at the work place than they had previously.

3.5 In particular about authorship

3.5.1 Some points of departure

The Commission sees the need for an introductory presentation of rules and practices related to issues linked to authorship on a more general level before commenting on individual circumstances.

Under this section, the Commission will first refer to the fact that the discussion on authorship, coauthorship and contributors within medical research is an old and continuously recurrent subject matter that has been the object of extensive discussions internationally for years. The question of who is the legitimate author of an article is one of the most discussed and controversial questions within medical publishing.18

Several arguments may be pleaded in favor of uniform rules for authorship.

In the first place the responsibility to readers including the scientific community presupposes that the person or persons stated as authors in fact can defend the message presented.

In the second place various requirements to and different practicing of rules relating to authorship may give an incorrect and unjust basis for comparisons within the system of merit in which scientific authorship plays the lead. One aspect in this connection is also funding systems within scientific research.

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where authorship is one criterion in relation to the granting of research support. In later years, the financial incentives related to such authorship have been reinforced by governments.

3.5.2 The Vancouver rules for medical publication

The so-called Vancouver rules or criteria\textsuperscript{19} are at the centre of the discussion on authorship within medical and health research. These standardized criteria were prepared under the auspices of a small group of editors of international medical journals, who met informally in Vancouver in 1978, with the aim of establishing guidelines for manuscripts delivered to the publications. The group, gradually becoming known as the Vancouver Group, published the guidelines initially in 1979. The Vancouver Group expanded and gradually developed into the International Committee of Medical Journal Editors (ICMJE) meeting annually. The criteria have been subject to continuous revisions. The Vancouver Group has been a small group without any real formal or legal status. In spite of this, the Vancouver Group has worked up an authoritative status enjoying the respect of researchers, academic institutions and public authorities globally. The authoritative force of the Vancouver rules can to a large degree be ascribed to the important medical journals represented in the Group, among them the American New England Journal of Medicine and Journal of the American Medical Association (JAMA), as well as the British Medical Journal (BMJ) and The Lancet.

The fundamental idea behind the Vancouver Group’s criteria for authorship is that authorship is an intellectual activity and that the ideas, analyses and not least the preparation of manuscript itself are the core of the scientific authorship.\textsuperscript{20}

This idea is in good harmony with the more general criteria for authorship and general copyright principles. It should be noted, however, that the Vancouver rules are not more stringent than more general criteria. On the contrary, the Vancouver rules have been subject to continuous adaptations which make them currently appear as relatively liberal, in the sense that for example data retrieval is now equal to idea/design and analysis/interpretation. By the revisions of the last 10 years, the Vancouver rules have also downgraded the responsibility to be borne by the individual author, see Annex 2. Whereas in 1997 they stated that “Each author should have participated sufficiently in the work to take public responsibility for the content”, later versions state that “Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content”. The 2003 version stated that “one or more authors shall take responsibility for the integrity of the work as a whole, from inception to published article”. In the 2006

\textsuperscript{19} Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication – updated February 2006

\textsuperscript{20} Nylenna M. Forfatterskapskriteriene er endret [The authorship criteria are changed]. Tidsskrift for Den Norske Lægeforening 2000;120:1844
version this responsibility is further weakened to “Some journals now also request that one of more authors, referred to as “guarantors”, be identified as the persons who take responsibility for the integrity of the work as a whole, from inception to published article, and publish that information”.

Thus the Vancouver rules may be considered as a definition of the more general authorship principles which apply generally in all fields. In other words, the criteria are adapted to the particular circumstances one believes exist in relation to medical research and publication of medical research results in medical journals. The authorship criteria are thereby not necessarily characteristic of the principles applying outside the medical professional area. In this context, the Commission in particular notes the new amendments of 2000 following a critical revision, in which to collect data was assigned a value, which together with writing and approving the manuscript may lead to authorship. The fact that supplying data material may qualify for authorship is, in the Commission’s view, related to this being widespread in the medical professional community, and that it is often a precondition for being able to perform medical and health research. To a large degree one is dependent on sub-suppliers who do not necessarily participate in the intellectual process of the research project and/or the publication of the research results but who nevertheless have a substantial role in the research project. They are necessary contributors for the research project being able to be implemented. This contribution and the expertise held by the sub-suppliers must in one way or another be rendered visible and valued. These factors, in combination with medical publications also having become an important element in the medical community, have resulted in a practice in which persons are credited for their efforts in the research projects through a coauthorship, without having necessarily contributed to any particular degree to the intellectual process and creation of the intellectual work itself which one associates with authorship in general. In many important medical studies it is not unusual that an article has from 20-50 coauthors. The typical contribution, which is in full compliance with the Vancouver rules, can then be contributions with patient or other data material as well as a critical review of a final manuscript and its approval. For many people, and then in particular the general public, it may appear as rather incomprehensible that one departs from the general perception of the authorship concept.

The authorship criteria stated in the Vancouver rules must be seen in light of medical research often being characterized by collaboration projects. One is often collaborating across professional areas, for example laboratories and statisticians collaborating with clinicians and epidemiologists. Cooperation also takes place across institutions, and not least across national borders. This leads to a split of areas of work and responsibility. These factors have been at the centre of the debate linked to coauthorship.
But such distribution of tasks may also contribute to pulverizing the responsibility. The Vancouver rules have taken this into consideration in that publication under the auspices of large research groups shall include one or several authors/coauthors assuming the primary responsibility for the publication and the project as a whole, in the same way as the project manager will have the primary responsibility for the planning, implementation and completion of the research project as a whole.

For the sake of completeness, the Commission finds it appropriate to include the key provisions in the Vancouver rules in their entirety, as they read per June 1, 2006:

“II. Ethical Considerations in the Conduct and Reporting of Research
 II.A Authorship and Contributorship
  II.A.1. Byline Authors

An “author” is generally considered to be someone who has made substantive intellectual contributions to a published study, and biomedical authorship continues to have important academic, social, and financial implications. (1) In the past, readers were rarely provided with information about contributions to studies from those listed as authors and in acknowledgments. (2) Some journals now request and publish information about the contributions of each person named as having participated in a submitted study, at least for original research. Editors are strongly encouraged to develop and implement a contributorship policy, as well as a policy on identifying who is responsible for the integrity of the work as a whole.

While contributorship and guarantorship policies obviously remove much of the ambiguity surrounding contributions, it leaves unresolved the question of the quantity and quality of contribution that qualify for authorship. The International Committee of Medical Journal Editors has recommended the following criteria for authorship; these criteria are still appropriate for those journals that distinguish authors from other contributors.

• Authorship credit should be based on 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.
• When a large, multi-center group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript (3). These individuals should fully meet the criteria for authorship defined above and editors will ask these individuals to complete journal-specific author and conflict of interest disclosure forms.

When submitting a group author manuscript, the corresponding author
should clearly indicate the preferred citation and should clearly identify all individual authors as well as the group name. Journals will generally list other members of the group in the acknowledgements. The National Library of Medicine indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript.

- Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.
- All persons designated as authors should qualify for authorship, and all those who qualify should be listed.
- Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Some journals now also request that one or more authors, referred to as “guarantors,” be identified as the persons who take responsibility for the integrity of the work as a whole, from inception to published article, and publish that information.

Increasingly, authorship of multi-center trials is attributed to a group. All members of the group who are named as authors should fully meet the above criteria for authorship.

The order of authorship on the byline should be a joint decision of the coauthors. Authors should be prepared to explain the order in which authors are listed.

II.A.2. Contributors Listed in Acknowledgments

All contributors who do not meet the criteria for authorship should be listed in an acknowledgments section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair who provided only general support. Editors should ask authors to disclose whether they had writing assistance and to identify the entity that paid for this assistance. Financial and material support should also be acknowledged.

Groups of persons who have contributed materially to the paper but whose contributions do not justify authorship may be listed under a heading such as “clinical investigators” or “participating investigators,” and their function or contribution should be described—for example, “served as scientific advisors,” “critically reviewed the study proposal,” “collected data,” or “provided and cared for study patients.”

Because readers may infer their endorsement of the data and conclusions, all persons must give written permission to be acknowledged.”
The Vancouver rules set forth three key conditions for coauthorship:

1) substantial contributions to conception and design, OR acquisition of data, OR analysis and interpretation of data,
2) drafting the article OR revising it critically for important intellectual content; and
3) final approval of the version to be published.

All three criteria must be met.

Table 1: The Vancouver rules’ main criteria for coauthorship

As shown by table 1, all three criteria must be met, but such that it is sufficient that one of the alternatives under 1 and 2 respectively have been met. This means that all the authors must have been involved in the intellectual process writing a scientific publication involves, see condition 2, and “the additional requirement” that all authors must have participated sufficiently in the work in order publicly to assume responsibility for suitable parts of the content of the publication. It must be underlined that these criteria have been under development. In Annex 2, the Commission has included a table showing how the key criteria looked at various points in time.

As can also be seen, the Vancouver rules differentiate between authors and contributors. Contributors who do not qualify as an author, by not meeting all three conditions, shall be stated and acknowledged in a separate section, “acknowledgement”. Examples of such contributors may be a person who assists solely in data collection, part analyses, technical help, writing assistance or more general support.

3.5.3 The relation of medical research to the Vancouver rules

The Vancouver rules do not legally represent any form of mandatory legislation. The criteria are in their nature guidelines which hold authority arising by the degree of compliance of the principles that take place in practice.

However, several of the publications referred to above show that the Vancouver rules to a varying degree are known among medical researchers, and that they also in a varying degree are accepted and practiced by the researchers who are familiar with the principles.

Based on the global impression the Commission has gained through its work, among other things, it seems that also within medical research in Norway, there are different perceptions of the authority of the Vancouver rules. The Commission’s impression is that the principles are not (or have not been) well
known in all research communities, although most people probably have “heard about” them. The Commission’s impression is also that the principles in certain research communities are practiced rather leniently.

The Commission underlines that these impressions are based on a limited material, but there is nevertheless reason to express these observations, in that it appears as obvious to the Commission that any such extensive deviating practicing – or non-practicing – of the Vancouver rules in a major part of the medical research community obviously will have to be taken into consideration when assessing whether there is a basis for criticism against the coauthors’ part in the case. The Commission’s impression at this point is moreover in harmony with the findings that are documented in international journals.

The Commission would in particular refer to a British study including 66 researchers which found that 76% supported criteria for authorship, but that few had any knowledge of or used available criteria. Of the five persons who could specify all three Vancouver rules, only one person knew that all three criteria are to be met.21

The study concluded that “there seems to be a gap between editors’ criteria for authorship and researchers’ practice”, and that “the strategy for communicating and implementing the criteria of the International Committee of Medical Journal Editors has largely failed. New initiatives should engage researchers and meet their legitimate needs. Future guidelines should be developed collaboratively and not be imposed on researchers by editors.”

Similar discrepancies between the Vancouver principles and that which is practiced in medical research communities in other countries have been documented in other articles.22

On the other hand, it is obvious that journals as well as research institutions must be able to practice and enforce the Vancouver rules as if they were binding, and not only guiding. That means that they may make demands that authors that publicize or work for them, follow these criteria. Thereby, the criteria will be seen as mandatory for these researchers. The management at the Radiumhospitalet, for example, has clearly stated to the Commission that the Vancouver rules apply to researchers at the institution, and that it is expected that they are followed. These requirements should be seen as a binding work instruction which the employer must be able to establish and enforce. However, it is unclear to the Commission whether this instruction has reached and is being practiced by the employees at the institution, and if so, to what degree.


3.5.4 The author responsibility

Based on the Vancouver rules and other rules for authorship, it may seem unclear what responsibility the individual author has when publishing research results. In the Commission’s opinion, this responsibility must be seen in the light of general liability rules, see section 3.3.

The implication for authors is that one must assume responsibility for what one has done, or as the case may be, not done, but ought to have done. Consequently, it is not necessarily the fact that one is mentioned as an author or coauthor that is decisive for the responsibility question but first and foremost what one in actual fact has done or not done. This also means that one must accept that individual authors are responsible for different elements, even when they act jointly, provided one is able to determine what the individual person has done. When several persons prepare a publication together, it is inherent in this that it is necessary to no little degree to build on and trust what a partner or other persons involved provide in the form of information of other parts of the research work. On the other hand it is of course possible that a coauthor or others will be held responsible because circumstances existed that indicated that one should have reacted and made further investigations.

However, to be an author does not imply that accepting (co-)authorship means almost signing a contract and becoming responsible for absolutely all parts of what is stated in the publication being correct. Such an interpretation has no basis or legitimacy in real life today, nor in the current version of the Vancouver rules, cf the requirement as to responsibility for “suitable parts”.

3.6 Retraction of invalid publications

Medical journals have customs for retraction of invalid publications that have been published. However, the rules for so-called retraction are neither uniform nor entirely clear, and such retraction occurs relatively seldom. In section III.B of the Vancouver group’s guidelines, the guidelines for corrections, retractions and expression of concern are stated as follows:

“III.B. Corrections, Retractions and "Expressions of Concern"

Editors must assume initially that authors are reporting work based on honest observations. Nevertheless, two types of difficulty may arise.

First, errors may be noted in published articles that require the publication of a correction or erratum of part of the work. The corrections should appear on a numbered page, be listed in the contents page, include the complete original citation, and link to the original article and vice versa if online. It is conceivable that an error could be so serious as to vitiate the entire body of the work, but this is unlikely and should be handled by editors and authors on an individual basis. Such an error should not be confused with inadequacies exposed by the emergence of new scientific information in the normal course of research. The latter require no corrections or withdrawals.
The second type of difficulty is scientific fraud. If substantial doubts arise about the honesty or integrity of work, either submitted or published, it is the editor’s responsibility to ensure that the question is appropriately pursued, usually by the authors’ sponsoring institution. However, it is not ordinarily the task of editors to conduct a full investigation or to make a determination; that responsibility lies with the institution where the work was done or with the funding agency. The editor should be promptly informed of the final decision, and if a fraudulent paper has been published, the journal must print a retraction. If this method of investigation does not result in a satisfactory conclusion, the editor may choose to conduct his or her own investigation. As an alternative to retraction, the editor may choose to publish an expression of concern about aspects of the conduct or integrity of the work. The retraction or expression of concern, so labeled, should appear on a numbered page in a prominent section of the print journal as well as in the online version, be listed in the contents page, and include in its heading the title of the original article. It should not simply be a letter to the editor. Ideally, the first author should be the same in the retraction as in the article, although under certain circumstances the editor may accept retractions by other responsible persons. The text of the retraction should explain why the article is being retracted and include a full original citation reference to it. The validity of previous work by the author of a fraudulent paper cannot be assumed. Editors may ask the author’s institution to assure them of the validity of earlier work published in their journals or to retract it. If this is not done editors may choose to publish an announcement expressing concern that the validity of previously published work is uncertain.”

3.7 In detail on education of researchers/training of researchers and the supervisor role

Since 1993, the national regulations called Regulations for PhD Degrees with Requirements as to an Organized Education of Researchers have formed a common basis for organized education of researchers in Norway. The organized researcher education implies that the traditional PhD in arts and sciences gradually is to be replaced by doctor degrees specific to special subjects, mandatory course teaching was introduced to make the researcher education wider, and the relationship between the PhD candidate and his/her supervisor was to be formalized through written agreements.

The universities have an overall responsibility for the education of researchers in Norway. Yet, an estimated third of the PhD candidates have their main place of work at other institutions, and to a considerable degree receive supervision by persons who are not employed at the universities. In addition to the PhD candidates’ own intellectual qualities, it is the supervisors’ and the research community to which the candidate is related that is of the most importance for the quality and efficiency in the education of researchers. The relation between supervisor and PhD candidate is here a crucial item.

Analyses of development in the organized education of researchers show large variations as regards adaptations to the common regulations, in its practicing, in the interpretation of the professional
requirements to a PhD degree, in attitudes to supervision and how the scope and organization of the course part is viewed. Variations are in particular related to various lingering subject-specific traditions, and tensions between the requirements as to an independent research effort and the requirements as to the supervisor’s contribution in the work with the dissertation often seem to arise.23

To be a research recruit means essentially to complete a researcher education with the achievement of a PhD degree as the final goal. Seen this way, the PhD candidate will be in an education situation, having a role with certain similarities to the role as a student.

On the other hand, the PhD candidate has completed his/her university education at master level, and he/she also often has a certain work experience. The main part of the PhD degree education consists in fact of more or less independent research. In this respect, the PhD degree student may be compared with ordinarily engaged scientific and/or clinical staff. This tends to make the research recruit’s position close to that of ordinary scientific employees regarding rights and obligations.

As a starting point it may therefore be natural to consider the recruits as students when they study and participate in courses/seminars and the like, and as employed scientific staff when they otherwise are engaged in research.

The personal responsibility of the recruits, however, must be decided concretely in relation to the individual situation. Some candidates work rather independently and appear as de facto project managers for their PhD degree project, for which they also have a considerable/the main responsibility for the planning, implementation and completion. Other recruits will often be in a far more subordinate relationship, in which typically the supervisor is also the project manager, co-researcher and holder of the day-to-day responsibility for the PhD candidates’ projects from inception to end, without this excluding a personal responsibility also for the recruit.

Thus, to be a supervisor is a central task in the education of researchers. In spite of the guidelines mentioned above, there are clearer and more unambiguous rules for the role of the supervisors as regards training in good research practice in a wide sense (vocational ethics for researchers). The supervisor role and the status held by the supervisor is to a large degree based on customs in the research communities, adapted to special circumstances at the individual institution, the individual professional and research community, and not least specific agreements between and circumstances related to the individual supervisor and/or candidate relationship. In the booklet PhD guidelines, an idea booklet prepared by three Danish medical researchers, the following is stated on page 8:

“The purpose of the guide is, in a master study situation, to inspire and comment on the PhD candidates’ personal effort and the work emerging thereof. In addition, as a supervisor one is to act as a personal

support. The aim of the guide is not primarily to disseminate knowledge relating to methods, but rather to be a catalyst for the candidates’ development as a researcher. … Supervising is a process, in which by a combination of inductive and deductive pedagogy shall help the PhD candidate to acknowledge problems and find solutions to them.”

These general remarks seem to have some relevance also in a Norwegian context.

The booklet also states that a supervisor is not necessarily the same as a project manager. The supervisor may of course be the project manager, but such a double function is not automatic.

Nor is it automatically so that as a supervisor, one is also to be a coauthor or last author on the candidate’s publications, although especially within the medical community a certain tradition for this has developed. The supervisor must like everybody else meet the criteria for authorship to be listed as an author.

Thus the supervisor will basically appear as an advisor and conversation partner, unless more committing responsibilities and rights follow from other circumstances, e.g. that the supervisor also is placed in the line above the candidate and is the closest superior of the latter.

Gradually it has become customary that when admitted to a PhD degree program, the candidate enters into a contract of professional direction in the PhD degree education. On the other hand, these contracts are often so vague that they provide little guidance beyond normal customs. In the absence of clear agreements and rules, the supervisor’s responsibilities and duties must therefore be determined specifically.

According to the PhD degree program at the Medical Faculty, University of Oslo (adopted June 14, 2005), for example, the following rules apply:

Section 8 Supervision
The PhD candidate and the supervisor shall be in regular contact. If the PhD candidate has several supervisors, a main supervisor with the primary responsibility for the professional follow-up of the PhD candidate shall be appointed.

At least one of the supervisors must be employed by the faculty at which the PhD degree candidate is admitted or at another entity at the university approved by the faculty. All supervisors shall have a PhD degree or corresponding professional competence. Both the (main) supervisor and PhD candidate are obligated to report in accordance with the regulations stipulated by the faculty.

The supervisor is, in consultation with the institution, responsible for arranging for the PhD degree candidate’s regular participation in an active research environment. For PhD degree candidates being associated to another institution, an agreement shall be entered into between the institution awarding the degree and the cooperating institution which shall regulate the working conditions which shall include ensuring the PhD degree candidate’s participation in an active research environment.

The frequency of the formalized supervisor contact (individual supervision and group supervision) shall be set forth in the agreement.

At least one supervisor is to be associated to the medical faculty at the University of Oslo.

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The supervisor shall:
- Advise on the formulation and delimitation of the subject and problem for discussion
- Discuss and consider hypotheses and methods
- Assist the candidate in finding his/her way in the relevant literature and raw data (library, archive, etc.)
- Discuss the arrangement and execution of the presentation (disposition, language, documentation, etc.)
- Keep updated on the progress of the candidate’s work and evaluate it in relation to the work plan
- Assist in introducing the candidate to relevant scientific environments
- Discuss results and their interpretation
- Guide the candidate in research-ethical questions related to the dissertation

The PhD degree candidate shall:
- Submit reports or drafts of parts of the dissertation to the supervisor in accordance with the PhD degree agreement
- In his/her work comply with the research ethical principles applicable to the subject area.

The parties are obliged continuously to inform one another of all matters of importance to the accomplishment of the PhD degree education. The parties are obliged to actively follow up circumstances that can cause a risk of a delayed or failing accomplishment of the PhD degree education, in order that the education as far as possible may be accomplished.

The PhD degree candidate and supervisor may, if they agree, ask the admitting body to appoint a new supervisor for the candidate.

If a PhD degree candidate or supervisor should find that the other party does not comply with his/her duties, the party alleging that there is a breach of obligations is obligated to bring this up with the other party. The candidate and supervisor shall jointly try to find a solution to the situation that has occurred.

If a PhD degree candidate or supervisor finds that the other party does not comply with his/her duties, and the parties’ following discussions have not agreed on how to solve the situation, the candidate or supervisor may ask to be released from the supervisor agreement. A request to be released from the supervisor agreement shall be addressed to the medical faculty and forwarded via the basic entity. A copy of the request shall be sent to the other party by the party bringing the case. Any decision to release the PhD degree candidate and supervisor from the supervisor agreement shall be made by the medical faculty.

It lies to the medical faculty to approve a change of supervisor when the supervisor or the PhD degree candidate has asked for such a replacement.

The supervisor may not in any case step down until a new supervisor has been appointed. Accordingly, in the application form for admission of Jon Sudbo on the PhD degree program in December 2000, an agreement was entered into on professional supervision with the following main elements:

5. THE SUPERVISION RELATIONSHIP
In the professional supervision, the supervisor shall in particular:

- Give advice on the formulation and delimitation of the subject and presentation of the problem
• Discuss and evaluate hypotheses and methods
• Give assistance in getting acquainted with literature and raw data (library, archives, etc.)
• Discuss the arrangement and preparation of the presentation (disposition, language, documentation, etc.)
• Keep informed of the progress of the candidate’s work and evaluate it in relation to the work plan
• Assist in introducing the candidate to relevant scientific environments
• Discuss results and their interpretation

The PhD candidate undertakes to submit reports or drafts of parts of the dissertation to the supervisor, as the case may be in connection with seminars, every ….

Both parties in the supervision relationship are entitled to regular contact and information on the progress of the work. The framework for this is to be determined by the body approving the annual progress report, cf item 4.

3.8 Retention of research material – obligation and right

3.8.1 The problem at issue

Material used in medical and health research often consists of human biological material (including biobanks), data files (including personal data registers), case notes, analyses, memos, draft manuscripts and the like. The research material is the basis for the research results. To enable a future check of whether the research results are correct and/or arrived at in a sound manner, it is often a prerequisite that the underlying research material can be examined.

In this context there can be question of, and if so, how and for how long, researchers must retain the research material (retention obligation).

Another problem is related to the retention right – i.e. the researcher’s right to manage the research material: May researchers delete research material whenever they want to, or keep the research material for as long as they wish and do with it as they themselves find serviceable?

Some rules and guidelines on this exist, but they are unclear and fragmented and for that reason fairly unknown.

3.8.2 The retention obligation

According to good scientific practice, raw material shall basically be retained in order to ensure checks. The period of retention according to scientific practice is difficult to state. For example, this norm is
specified in the Regulations on Clinical Testing of Medicines, in which section 5-3 (2) and (3) state that it must be ensured that source data are available at the place of testing for at least fifteen years from the date of the final test report. The Nylenna Committee has also recommended the enactment of a retention obligation for all raw material for ten years after the completion of the research project (NOU 2005:1). In addition, there are relevant rules on this in the Bio Bank Act, the Personal Data Act and the Personal Health Data Filing System Act, which the Commission does not find reason to comment on in detail. There are also rules for the retention and processing of documents in the health service in, i.a., the Specialist Health Service Act, the Health Personnel Act and the Patient Case Notes Regulations. The employer may also have established internal instructions on this. Moreover, documents prepared by employed researchers at public institutions, as for example a public hospital, even if it is not practiced like that currently, may be subject to more general rules on the retention and processing of documents as for example the Archives Act. The retention obligation must of course take appropriate account of the requirements made to the processing and storing of person-identifiable information.

As an example may also be mentioned that the Research Council of Norway in its standard form contract provides that the research material shall be stored in line with good scientific practice. The prevailing contractual condition “Standard form contracts and granting letters – R&D” state among other things:

“Unless otherwise provided by the body authorized to decide the use of the data, copies of all research-generated data, including necessary documentation, shall be transferred to the Norwegian Social Science Data Services. Such transfer shall take place as soon as possible, and no later than two years after the conclusion of the period to which the project grants apply. The data that are to be comprised by this must be agreed specifically with the Research Council. … The person responsible for the project is responsible for following relevant standards of quality, statutes and other public regulations. Where test persons/patients/clients are included in research projects, a recommendation by the regional committee for Medical Research Ethics according to the prevailing rules relating to the obligation to submit is required. The project-responsible person is responsible for the recommendation being complied with. … The project-responsible person shall file the final test report in an adequate way for a minimum of ten years after the completion of the project. The project-responsible person is under a duty to ensure that the data are stored in such a way that they will also be taken care of and be available should the project-responsible person cease to have such a responsibility. The project-responsible person is obligated to follow recognized quality norms when collecting and filing data. Any breach of obligations relating to the reporting and filing will be considered as a fundamental breach and thus give the Research Council reason to cancel the contract, cf section 12.2. …”

Since 1995, the Research Council has had an agreement with the Norwegian Social Science Data Services on the filing of research data relating to medical and health research. For the year 2000 this included that “The project-responsible person shall file the final test report and project data in an adequate way for a minimum of ten years after the conclusion of the project. The project responsible-person is under a duty to
ensure that the data are kept in such a way that they will also be taken care of and be available if the project-responsible person is dissolved” (read: the institution).

3.8.3 Right of retention and management

As regards the question of the right of management in more general terms, reference is made to the fact that research material, and in particular the use and retention of human biological material and personal data, collected by or under the auspices of a research institution, will, as the obvious main rule, be subject to the institution’s overall responsibility, and thus also to the institution’s right of management. This type of sensitive material is not the private property of an employed researcher. This must now be fairly clear, although a district court decision from 1999 may be cited in support of the opposite solution.

27 Simonsen S, Nylenna M. Helseforskningsrett [Health Research Law] Oslo: Gyldendal, 2005
4. **Clarification of the facts**

4.1 *The cause – the Lancet article*

In December 2005, Camilla Stoltenberg, Division Director at the Norwegian Institute of Public Health, read an article published by a group of Norwegian and foreign researchers in the internationally highly respected journal *The Lancet* in October the same year:


While reading the article, Stoltenberg became aware of certain cited factors which she was not able to see agreed with actual facts. This was discussed with other researchers at the Institute of Public Health. The Cancer Registry, which had been stated as supplier of the cancer cases, was also contacted. The Cancer Registry further contacted Professor Lars Vatten, MD, of the Norwegian University of Science and Technology (NTNU). Vatten is among other things a member of the management group for Cohort of Norway (CONOR), to which a reference was also made in the article. CONOR is both the designation of a collection of health data and blood samples, and a collaboration between the Public Health Institute and the universities relating to regional health studies. In addition, Vatten is involved in HUNT (the Nord-Trøndelag health study). Vatten read the article and reacted to several of the discrepancies in relation to actual facts. He brought this up in an email which was sent to the first author, Jon Sudbø, on January 5, 2006. On January 10, a meeting was held with Jon Sudbø and Albrecht Reith at the Cancer Registry, at which Vatten among other persons was present. On January 12, Jon Sudbø admitted to his superiors at the Radiumhospitalet that he had fabricated the data file on which the research results presented in the Lancet article was based. This means that the alleged patients from whom the analyzed data originated, were fictitious. Jon Sudbø has later on confirmed this to the Commission. Jon Sudbø has also stated that there are deficiencies in two other articles:


The Lancet article has subsequently been retracted. Journal editors have issued so-called expressions of concern regarding the articles in Journal of Clinical Oncology 2005 and New England Journal of Medicine 2004, as well as two articles by Sudbø et al published in the same journals in 2002 and 2001 respectively.28

On this background, the Commission found reason to investigate the entire scientific activity and production of Jon Sudbø. The Commission also found reason to investigate the role of all the coauthors and other players.

The Commission’s primary task has been to map the material which forms the basis for the publications. Important questions have been:

- Are the patients who allegedly have been studied real or fictitious?
- Have patient data been manipulated?
- Do serious methodological flaws exist?
- Are there evident and serious flaws in the research reporting?
- Are there other serious breaches of scientific practice/good research practice?

In line with these points of departure, the Commission started its work by mapping the data basis which is the foundation of Jon Sudbø’s first big scientific project, the PhD degree project. The background for this choice is that the raw material collected in connection with the PhD degree project, as well as the results thereof, has been used in and forms the basis also for Sudbø’s subsequent research.

Jon Sudbø has been presented with the draft report, i.e. what corresponds to Chapter 4 through section 7.2.1 of the prevailing report on two occasions. In a letter of May 30, 2006, he submitted a series of comments to the first draft report which the Commission has compared with information which otherwise has come to light during the investigation. The Commission has corrected the draft on points where one found a factual basis for taking account of Sudbø’s comments. However, the Commission would emphasize that these comments have not entailed any significant changes in the Commission’s assessment of the validity of Sudbø’s research work. A substantial part of Sudbø’s objections are linked to the relationship between him and his supervisor, Reith, in that Sudbø alleges that the supervisor had a much more key role in the research project than the impression the Commission has got through the investigation otherwise. The Commission

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will at some places comment on diverging perceptions of the facts where this is deemed necessary. Sudbø chose not to comment on the revised draft report, sent to him subsequently.

4.2 The PhD degree project relating to oral cancer

4.2.1 Introduction

Jon Sudbø is educated as a dentist (cand. odont.) from 1985 and medical practitioner (cand. med.) from 1994 with the very best grades. In his odontology study he came best in his class. In 1993 Sudbø, in cooperation with Professor Albrecht Reith, MD, at the Radium hospitalet applied to the Cancer Society of Norway for funding of his PhD degree project. The study concerned finding methods to predict oral cancer. Sudbø has stated that it was Albrecht Reith who took the initiative to the project at issue. This took place by Reith making contact with Associate Professor T.Ingar Leidal at the Faculty of Odontology at the University of Oslo, to ask him to recruit a candidate to a research project on oral premalignant diseases, which Reith had been planning for some time. After this first contact in February 1993, Sudbø was contacted by Leidal, who thought Sudbø might be suited for such a project. However, Sudbø had not previously worked with this problem, which he found interesting. The first contact between Sudbø and Reith took place in February or early March 1993. The Cancer Society granted Sudbø a three year stipend, with Albrecht Reith as main supervisor. Sudbø was then from 1994 paid a salary as a recruitment fellow by the Cancer Society.

4.2.2 The subject matter of the doctor degree project

Background: No methods exist to indicate which oral dysplasias may also develop into cancer.

Goal I: The project description from 1993 states that Sudbø and Reith wanted to study the malignant transformation potential through a historical prospective study of leukoplakia materials, in order to map out any structural DNA changes in dysplasias, and compare these findings with the persons who later on developed cancer. They also wanted to start a prospective study. The aim was to be able to say something about the prognosis of premalignant conditions. Image analysis methods were also to be tested. The material for the historical prospective study was according to the project description already available, whereas the material for the prospective study was to be obtained by scraping of suspicious mucous areas.

Goal II: In addition they wanted to study manifest cancers. The hope was to map out the DNA changes which identify cancers with a good and poor prognosis. The project description states that the material had
been collected. Sudbø has stated that he is unable to understand that the project description states that the material had already been collected. He alleges that there is no doubt that this material was collected after he started as a recruitment fellow. The Commission finds it predominantly likely that Sudbø, in a project which he had just heard about a few weeks before, did not at this point in time have the opportunity to collect the material in advance. Sudbø assumes that the project description is formulated to reflect that the project had been prepared by Reith. The Commission finds, and this is supported by Reith, that the formulation in the project description reflects the fact that Reith through his contacts had knowledge about the material that had been collected at Gade’s Institute (and possibly also the material from the faculty of odontology), to which the Commission will revert later on.

4.2.3 The organization of the PhD project

Jon Sudbø’s PhD project was carried out during the period 1993-2001. The PhD project has a rather unclear, but at that time hardly unusual, basis and organizational structure, which the Commission has seen reason to try to clarify and to which it will relate some remarks. The organization of the PhD project and the formalities in that connection, is, i.a., of great importance to the everyday as well as the overall responsibility for the planning, implementation and completion (reporting) of the project.

Jon Sudbø first received stipend funds from the Cancer Society from January 1st 1994 till December 31st 1996. In 1996 he was in addition granted a finalizing year. During this period, the Cancer Society formally was his employer. As from August 1, 1996 until January 19, 1998, Sudbo obtained a leave of absence to complete his internship. In addition, he ran his own private dentist practice at Årvoll Dentist Center sharing an office with some colleagues.

During the two first years, Sudbø did not have a formal employment relationship at Radiumhospitalet. But his main supervisor – Albrecht Reith – was employed as a researcher at the department of pathology, division for digital pathology. According to the usual practice when projects were financed externally, office space and the practical organization of Jon Sudbø’s work were arranged at this department. From January to September 2000, Sudbø received a stipend from the cancer research institute at the Radiumhospitalet, and he was then formally temporarily employed at the Radiumhospitalet. The head of the department of pathology was, and is, Professor Jahn Nesland MD. Professor Håvard Danielsen PhD was head of section at the division for digital pathology.

Sudbø has expressed surprise that he did not have any formal employment relationship at the Radiumhospitalet the first years when he worked at the department of pathology, among other things.
because Jahn M. Nesland in his capacity as departmental chief physician recommended the application to the Cancer Society. He also alleges that it was not until 2005 that he realized that Reith was not a professor at the University of Oslo.

In any case, it is a fact that Jon Sudbø and Reith performed their daily work at the Radiumhospitalet, and that the research took place there. This fact was known and accepted by the Radiumhospitalet. The Commission will also point out, as stated by Reith, that Sudbø’s PhD work was a continuation of three other PhD works which Reith had supervised prior to Sudbø’s project, and that these four projects, which were all supported by the Cancer Society, were concentrated on the same matter – the connection between early stages of cancer and subsequently developed cancer.

Thus, the Commission finds that the real association with the Radiumhospitalet appears as so strong that in reality one is dealing with an association relationship which is fully comparable with an employment relationship. Accordingly, the Commission finds that the Radiumhospitalet has had a customary daily management and instruction right in relation to Jon Sudbø during the entire PhD period, and that the research has taken place under the auspices of the Radiumhospitalet. Most of the conversations with the Commission are clearly indicative of this. It is also, for example, evident that both Gade’s Institute in Bergen and the Cancer Registry related to the Radiumhospitalet as an institution, and not to Jon Sudbø as a private person. The latter would also be contrary to expectations.

The Commission thus finds that the Radiumhospitalet had the primary responsibility for Jon Sudbø’s research.

It was not until November 2000 that Sudbø applied for admission to the PhD program at the University of Oslo. It was then fairly obvious that the dissertation was already as good as completed. When the management of the University of Oslo informed Sudbø of the fact that he had not been admitted to the program, he brought this up with Reith, who according to Sudbø’s statement made the excuse that it was all an oversight. Sudbø has underlined that he – in spite of failing to be admitted to the PhD program – had participated “in all the mandatory research education courses” and that these were paid for by the Radiumhospitalet. The Commission has not found it serviceable to deal with this in more detail.

Sudbø was admitted to the program at the end of December of the same year, at the same time as the dissertation was submitted. Sudbø’s dissertation was approved on February 20, 2001. The presentation of the thesis took place on March 9, 2001, and he was created a doctor in June, 2001. The main supervisor was Albrecht Reith. Since Reith was not a professor at the University of Oslo, Jahn Nesland, who held a professor II position at the University of Oslo, was appointed so-called contact supervisor. Nesland was the only one at the department who had such link to the University of Oslo, and he therefore held a series of such administrative positions. His position as contact supervisor was, in other words, established for formal reasons, by Nesland acting as the connecting link between the University of Oslo and Sudbø. Real supervision by Nesland was not an issue to any particular degree. Consequently, Nesland is not a coauthor of any of the publications resulting from the PhD project. The University of Oslo has thus primarily been
responsible for the approval of the dissertation and the thesis. The Cancer Society has exclusively acted as a funding source, and has not had anything to do with the organization and implementation of the project.

Conversations with the Commission clearly indicate that Jon Sudbø had a relatively free position as a fellow, a situation that is not unusual. Sudbø is described as clever, ambitious, experienced and independent compared with other fellows. Reith had a wide network which was used to obtain patient material among other things. Sudbø and Reith had a close relationship, with almost daily contact, during which professional questions seem to have been regularly discussed, although on a more general level. Reith has thus obviously been more peripheral in relation to being involved in the data material, data analyses and the like. Consequently, Reith’s role appears more as an active mentor than a co-researcher, see section 3.7 above.

However, Sudbø has denied that he had such a free position. He has alleged that his work efforts “clearly were directed by Albrecht Reith” and believes that it is not correct that Reith’s role can be described as a mentor role. Sudbø believes he can support this by referring to his work effort, when he took up the position in 1994, being directed towards work with graph theory analysis on carcinoma, first prostate carcinoma and subsequently oral carcinoma. Sudbø points out that this was not at all comprised by the original project description. Sudbø has alleged that when he commented on this to Reith, he was told that he should nevertheless commence with this work, and that one could later on revert to the work related to the original project description. Thus, Sudbø is of the opinion that Reith redefined Sudbø’s research project in the direction of method development. The reason for this change is allegedly that Reith had invited a French researcher to the Radiumhospitalet, Raphael Marcelpoil, as a post doc. for 12 months, after Reith having been an evaluator at Marcelpoil’s presentation of his thesis in 1993. Sudbø has alleged that the work with the graph theory analysis represented the entirely dominating part of his research effort up to 1999. The Commission understands Sudbø to believe that in this work he was dependant on cooperation with others to such a degree that this does not give grounds for finding that he had a free and independent position as a research fellow, nor that Reith had a withdrawn role as supervisor. The Commission moreover understands Sudbø such that the work that was comprised by the original project description (oral premalignant diseases), and which was to comprise analyses of the material from Gade’s Institute and the Faculty of Odontology at the University of Oslo, was not given priority in the period up to 1999. Reith refutes however that he is supposed to have instructed Sudbø to give priority to the work with the graph theory, and that this in all essentials was Sudbø’s priority. This explanation is clearly supported by a memo written by Sudbø in 2000, in which is stated that “it appeared absolutely obvious to the undersigned [Jon Sudbø] during most of my time as a research fellow that these methods [the graph theory] sooner or later would provide results, which was the reason I continued to
work with them, although Reith and the undersigned several times discussed my priorities in this respect”.

In spite of Reith’s close contact with Jon Sudbø, and Sudbø’s description of this relationship later on, to the Commission the project first and foremost appears as Sudbø’s own project, in which he himself took care of the everyday research. It seems as if it is he alone who in fact had the full control of the research project, including the research material that came from Gade and the Faculty of Odontology, see also the letter from Sudbø to the Cancer Registry dated February 20, 1996, cited under section 4.2.7, and the letter of reply of March 22, 1996.

Accordingly, the Commission finds that Jon Sudbø de facto was the project manager for the PhD project, a description with which Sudbø strongly disagree. The Commission also finds that Albrecht Reith has been the supervisor and mentor for the project.

The responsibility thus seems divided with the individual person/institution having an independent responsibility. The individual person’s/institution’s detailed responsibilities, and what they consist of, will vary, and for that reason they must be assessed specifically.

The Commission notes that the fact that responsibilities apparently have been relatively unclear and unheeded in this case, is first and foremost an institutional management responsibility.

4.2.4 Advance assessment of the PhD project

Three independent central requirements to the advance assessment of research projects are relevant in this case.

1. Duty of secrecy

The first requirement is related to access to personal data subject to secrecy (patient data/health information). The treatment of such information is as the main rule dependent on the consent of the patient to which the information applies. There are several exceptions. One exception, which is particularly relevant, is dispensation from the duty of secrecy in connection with research. These rules have been unchanged at least for the last ten years. Subsections 1 and 2 of the Medical Practitioners Act of June 13, 1980 no 42 section 36 on “Anonymity – research” read at that time:

“Medical practitioners may without regard to the pledge of secrecy communicate information that would otherwise be subject to secrecy concerning physical conditions or illness if individual characteristics have been deleted or changed so that the anonymity of the person concerned is protected. The Ministry may decide that information may or must be communicated for the purposes of medical research, and that this may be done without regard for the pledge of secrecy.”

See otherwise the Medical Practitioners Act section 31 (the main rule on secrecy) and the corresponding provisions in the then applicable Dentists Act of June 13, 1980 no 43 sections 31 and 36, as well as the Public Administration Act sections 13 and 13d. The Public Administration Act is unamended, whereas the provisions of the Medical Practitioners Act and the Dentists Act have been repealed but reenacted in sections
21 and 29 of the Health Personnel Act. Any dispensation from the duty of secrecy must be applied for in advance. Consent was previously given by the Norwegian Board of Health, but after January 1, 2002, this authority has been delegated from the Ministry of Health and Care Services to the Directorate for Health and Social Affairs.

It is a fact that Sudbø’s and Reith’s oral cavity project implied the collection and processing of sensitive patient information subject to secrecy. The Commission has not found any indications that any participant’s consent or dispensation from the duty of secrecy exists or that other relevant exemptions have been complied with. This means that this data processing is contrary to the then prevailing set of rules.

In this context it should be noted that research institutions and the like of course are not free to release patient information to researchers. This follows from the fact that patient information is subject to secrecy. Thus this is not only of importance to those who obtained unauthorized access to information subject to secrecy, but also for those who released patient information.

2. Personal data protection
Another requirement is related to the processing of personal data and creation of personal data registries in general. The main rule here is that such data processing requires a notification to or licence by the Data Inspectorate. A notification of application for a licence can also be sent via the personal data representative, if the research institution has one, in practice that will often mean the Norwegian Social Science Data Services (NSD).

It is a fact that Sudbø and Reith by collecting patient information from various institutions created a personal data registry with information that was partly highly sensitive. This data processing probably required a licence, a fact the Commission has received confirmation of from the Data Inspectorate and the NSD. There are no grounds to believe that Sudbø or Reith has applied to the Data Inspectorate or the NSD for such a licence.

3. Ethical assessment
A third requirement which is primarily a research-ethical requirement, but which increasingly is becoming a legal requirement, is the principle that medical or health research projects are to be assessed in advance by a regional research ethical committee (REC). This has been the system in Norway since the establishment of
the committees in 1985, but nevertheless such that the duty to submit for advance assessment gradually has been tightened up.\textsuperscript{29}

It is a fact that Sudbø’s PhD project was never submitted to REC-South (which would have been the correct body), not by Reith either. At its inception in the 1980’s it seems that mainly it was only invasive studies, i.e. studies in which one exposes patients or other research participants to some form of intervention/influence, which was comprised by a research-ethical obligation to submit. The Commission therefore found reason to put the question of whether Sudbø’s PhD project \textit{ought} to have been submitted for research ethical approval.

In that connection, the Commission made an inquiry to REC-South to have clarified which rules existed in 1994 when the project was started. REC-South then stated on a general basis, without having been sent either the project description or other documents, that:

“if the fact is that in this study, “register data was collected and linked with patient data” and that “biological samples were analyzed and telephone calls were made to patients for supplemental information on the use of tobacco where data were lacking”, then there is no doubt that the study should have been submitted to REC (Regional Committee for Medical Research Ethics). For a study with registry data it would suffice to have the approval of the Data Inspectorate, but where patient data, patient journals, biological data from patients, contact with patients per telephone to obtain information, etc., were concerned, it is obvious that it should have been submitted to REC.”

This fact must be seen in the light of the fact that far from all medical research projects of this type were submitted to the Regional Committee for Medical Research Ethics at that time, when probably also a justified doubt about the extent of the obligation to submit prevailed.

Failing compliance with the type of formalities we discuss here was hardly particularly unusual at that time. This is probably related to the fact that the set of rules was not well known. Improvements have probably taken place here by an increasing awareness of the set of rules among researcher, research institutions and regulatory bodies. It is likely that there is a certain connection here with discussions relating to formalities and the applicable set of rules in the wake of the BioBank Act which came into force on July 1, 2003, the Nylenna committee’s report from December 2004 (NOU 2005:1), the proposed enactment of the ethical committees and a national dishonesty committee, and the consultations that have been held in connection with these proposals for legislation. However, the Data Inspectorate in 2004 discovered that only one out of 30 medical and health research projects had routines that ensured that the legislation on personal

\textsuperscript{29} Refer to, \textit{i.a.}, an article by Bergsjø P. \textit{Biomedisinske forskningsprosjekter hvor forsøk på mennesker inngår – hva er nå det?} \textit{[Biomedical research projects of which experiments on humans form part – what would that be?] Tidsskrift for Den norske lægeforening}, 1993;113: 1443-1444.
data was complied with, and 11 out of 28 projects did not comply with the licence requirements. The obligation to delete was seldom observed, and in close to half of the projects the requirements as to consent were not fully met.\(^3\)

**The duty to submit**

It may be asked who was responsible for the formalities applicable to Jon Sudbø’s PhD project being in order.

In his statement to the Commission, Jon Sudbø asserted that he considered it to be his supervisor’s duty and responsibility to ensure that the formalities were in order. There may be something to be said for this point of view, since it is relatively usual that the main supervisor assumes the responsibility for and/or calls attention to the need of advance approval. On the other hand, it will often be natural to involve a research fellow in such a process, particularly where an independent project in which the fellow acts as the de facto project manager, is concerned. Then it will normally be the fellow who has the best knowledge of the project, through the closer proximity to it, even if it is the main supervisor who signs the application as such and other documents related to the project.

Sudbø however points out that most of the time up to 1999 was spent on method development, and this was work that allegedly did not require any form of approval by public bodies, and that it was a project that he alleges was ordered by Reith, and which was not comprised by the original application to the Cancer Society. On this basis, Sudbø denies that he was to be considered the project manager. It is true that Sudbø admits that in parallel with this, clinical material was collected, but this took place under the auspices of his supervisor, and then it must be natural to require that the supervisor assumes the responsibility to ensure that the research project complies with the set of rules – particularly in a situation in which Sudbø by his supervisor was ordered to work with an entirely other project which he experienced as demanding.

The compliance with the set of rules to which a research activity is subject, and the principles related to good research practice, is nevertheless also to be an important part of the researcher education. In this respect, Jon Sudbø ought to have been aware of whether these factors had been complied with or not. In line with the views accounted for in section 3.7, the Commission finds that a fellow as the main rule must have a certain independent responsibility to make sure that important factors like approvals, licences and other formalities (e.g. participant’s consent) are in order. This is particularly so where the fellow has such an independent position as in this case, where he probably is the only one who had the full daily control of the project. This responsibility is a personal and independent responsibility applicable regardless of the supervisor’s and institution’s independent responsibility.

Here is to be noted, although the Commission has not found reason to pursue the matter, that Jon Sudbø, having completed the PhD project, as far as the Commission can see, did not take care of notification to relevant bodies such as the Regional Committee for Medical Research Ethics, the Norwegian Social Science Data Services, and the Directorate for Health and Social Affairs in connection with other research projects, including projects in which he was a supervisor. One exception exists: the so-called PROTOCOL study, see sections 4.3 and 5.3. On the other hand, Sudbø in the protocol for the stated study and other articles demonstrates a good knowledge of the formal requirements relating to this type of research in Norway, as regards participant’s consent and advance assessment of research projects, among other things.

One problem, which is hardly unique in this case, seems to be a more or less unintentional and unfortunate mix of the role as a clinician (treating health staff) and researcher, in which the clinician’s access to patients and patient data for research purposes is unlawfully exploited, without the formalities being in order. It is of course a positive thing that clinicians carry on research, but the combination of different roles requires openness and awareness as regards the set of rules for the respective roles in order to avoid an unfortunate mix of roles.

The main supervisor, Albrecht Reith, states that he was not aware of these rules and requirements about an ethical advance assessment and licence by the Data Inspectorate, etc. For that reason he did not see it as his task to provide for an advance assessment either. In the Commission’s view, the main supervisor normally has an independent responsibility to ensure that formalities of this nature are in order before the fellow starts the research itself, either by taking care of it himself or by instructing the fellow to bring it in order. Sudbø has stated that he has difficulties in following the Commission’s considerations relating to the mix of roles as a clinician and researcher.

Furthermore, it must be a responsibility for the research institutions to ensure that research projects are assessed in advance and otherwise satisfy other formal requirements. However, the Commission has got the impression that the institutions, neither the Radiumhospitalet nor the University of Oslo, have seen it as their task to check that research projects are in fact initiated and implemented in accordance with statutes, regulations or work instructions. The Commission has got the impression that the education as well as the practicing of this has not been as good as it should be at the Radiumhospitalet.

On the other hand, the Radiumhospitalet in the last 10-20 years has issued increasingly better instructions and the like as regards research on patients and patient material, i.a. with special intranet sites and a support office for clinical research (www.klinforsk.no). Nevertheless, it appears to the Commission that there has been a lack of efficient routines and internal control at the institution which could have contributed to ensuring that statutes and work instructions in fact were known among the employees and were complied with. In other words, the problem was the implementation and practicing itself of external
regulations and internal instructions. Sudbo’s PhD project was never submitted to the Radiumhospitalet’s Protocol Committee, for example. The guidelines from 1998 state that the Protocol Committee “shall evaluate all types of clinical research projects wanted to be performed at the Radiumhospitalet and which in one way or another involve patients or patient material. The Protocol Committee may also on its own initiative bring up cases which have not been submitted to the Committee if it may seem as if it should have been submitted.” No one seems to have seen it as their responsibility to take care of any submission to the Protocol Committee.

Reference is further made to the fact that the research fellow was not required to submit documentation that the formalities were in order when he presented his thesis in 2001. It ought to be a simple and not very burdensome matter to require the submission of a protocol from the Regional Committee for Medical Research Ethics, licence from the Data Inspectorate, dispensation from the duty of secrecy, etc., together with a statement that research-ethical rules and guidelines have been complied with. The Commission has not found any reference to such rules in the PhD regulations or research fellow contract.

Although an advance assessment had not necessarily prevented other breaches of good research practice, such a review would nevertheless, in the Commission’s view, have been quality assuring and awareness raising. The lack of advance assessment increases the risk of breach of the patients’ integrity and is a threat to the population’s trust in research. Furthermore, it is difficult for institutions to safeguard completely against dishonest researchers sidestepping the system and omitting to comply with formal rules and instructions. The system must necessarily be based on a certain degree of trust.

In spite of the Commission’s limited basic material, it is nevertheless evident to the Commission that such obvious effects are linked to the institutional culture and system at the time as regards the institution’s and employed researchers’ attitude to the formalities, as for example the protection of personal data, that one must be able to characterize this as a system failure. The Commission has been informed of which measures are now prevailing, and has got the impression that this is a “problem area” which the management at the Rikshospitalet-Radiumhospitalet MC takes seriously. It seems as if this is an ongoing area of concentration with reinforcement and implementation of several good measures.

### 4.2.5 Reporting and publication of the PhD work

The PhD project can be divided in two.

The first part was carried out partly in cooperation with a post.doc. from France. This part comprises three scientific publications from 2000 which can be linked to method development and image analyses of tissue architecture based on raw material originating from Germany. In the Commission’s opinion, these studies are of a less sensational nature from a scientific point of view than the main part of the PhD project. However, as accounted for in section 4.2.3, Sudbo disagrees entirely in these works having a less essential role, even if
there has been less attention surrounding these studies than the main part of the PhD project. Sudbø underlines that these studies in terms of time and work represented the main part of his PhD work, and that they are published in recognized journals. The Commission has evaluated the articles and has not found indications of errors or deficiencies related to them.


Sudbø J, Ried T, Bryne M, Kildal W, Danielsen H, Reith A.

The articles are based on the same patient material and must be seen in conjunction. The patient material was probably obtained by Sudbø and Reith in 1995-1996 and linked with Cancer Registry data for supplementary information in 1996. The data material and samples were thereupon probably analyzed in 1999. The publication and the dissertation were published in 2001.

This patient material and the findings presented in the publications mentioned are at the very center of Sudbø’s subsequent scientific career and the series of subsequent publications.

The six articles were then collected in the PhD dissertation itself, which also contains an independent compilation and explanation of the PhD project. Thus it is the three latter articles together with the dissertation itself and the patient material these are based on, which have been the subject of thorough investigations that will be described below. The starting point is the dissertation itself.

4.2.6 The patient material – an overview

It appears from figure 5 at page 40 in the PhD dissertation, included as figure 1 in this report, that Sudbø started using human biological material (paraffin blocks with biopsy samples, tissue specimens, etc.) and person-identifiable data from 263 patients (cases). In essential, the patient material, according to New England Journal of Medicine 2001 and J Pathol 2001 as well as statements to the Commission, was obtained in the following way:
• Patient material from Pathological Laboratory, the Faculty of Odontology, the University of Oslo (hereinafter: the Odontology)

• Patient material from the Department of Pathology (“Gade’s Institute”), the Faculty of Odontology, the University of Bergen (hereinafter: Gade)

• Patient data from Gade and the Odontology were thereafter sent collectively to the Cancer Registry for linkage, i.e. a supplement of further data.

The Commission, on its part, has collected extensive documentation in the form of original and processed data files from various persons and instances, as well as statements before the Commission. The Commission has also made its own comparison of different data files in order to trace patients, tissue samples, check mutual linkage, etc., as part of its own internal control. The Cancer Registry has made similar investigations. The Commission was given access to the Cancer Registry’s very thorough investigations. By this, the Commission has clarified how the patient material for the PhD work was obtained, and how it originally looked, including which patients were included in the study and their disease history.

The Commission then compared a series of figures and facts presented in the publications to figures and facts in the Commission’s possession.

In the following, the Commission will point out along the way the errors, deficiencies and discrepancies discovered in the three mentioned articles and the dissertation itself, including the raw material on which these publications are stated to be based upon.
Figure 1 is taken from Jon Sudbø's PhD dissertation and shows, among other things, the inclusion process. An almost corresponding figure is included in New England Journal of Medicine 2001.

Figure 3
A flow chart showing the clinical material of oral premalignant lesions, and its use in Papers I-III. Forty-six cases originally included in Paper II, but one case was excluded, as it was regarded as an outlier because it was histologically classified as oral mucosa and integument by 2 observers.
4.2.7 Representation of the raw material in the publications

The total number

The dissertation states that originally one had access to material from 263 persons collected during the period 1976-1995. According to the articles and the dissertation, this material originated exclusively from archives at the Odontology and Gade.

This means that Sudbø originally had access to human biological material and personal data from altogether 263 different persons. The number of samples and tissue blocks and the like was much higher, however, because normally one has several samples and blocks from the same patient. Oncology 2001 refers to all 263 patients because it includes both leukoplakias (white patches in the oral cavity) and erythroplakias (red patches in the oral cavity). In New England Journal of Medicine 2001, this starting point is reduced to 242 (263-21) because patients with erythroplakias were excluded initially. In J Pathol 2001 the starting point is 196 (263-(21+46)), although this number is 217 in the dissertation. According to Sudbø, however, it was only for 196 persons that ploidy classification existed and which for that reason were treated in J Pathol 2001.

Below, the Commission will try to identify when and from where these patients come and the qualities they possess.

The time interval

In New England Journal of Medicine 2001 it is stated that the material originates from the period 1982 to 1995, whereas in the two other articles and in the dissertation it is stated to originate from 1976 to 1995. The correct time interval is unclear. According to the Cancer Registry it is supposed to be 1976 to 1995. In a letter from February 1, 1996 from Sudbø and Reith to Gisle Bang at Gade, it is stated that the material from the Odontology originates from 1984-89. In an undated letter, probably from the beginning of 1996, from Bang to Reith and Sudbø reference is made to the Gade material originating from 1981-95. In a letter from Sudbø to the Cancer Registry dated February 20, 1996, it is referred to the patients having been diagnosed 1984 up to 1995. It is surprising to the Commission that there is no conformity between the years stated. Nor is there any conformity between the stated period of time for collection in New England Journal of Medicine 2001 and the other articles.

Sudbø has denied to the Commission that there are discrepancies and “obvious errors” in the various datings, and has alleged that the total material is from 1976-1995, and that it is probable that some blocks taken before 1982 have been excluded because prior to 1982 it was not usual to use buffered formalin at the fixation of tissue blocks, which are less suited to hydrolysis and Feulgen coloring.
The ambiguities existing in relation to the time intervals are however, in the Commission’s opinion, inaccuracies of such a nature that they are apt to impair the reliability of the publications.

The material from the Odontology

Sudbø states that via Reith he got access to patient material from the Odontology represented by Hanna S. Koppang. Reith has stated that he, as far as he can recall, asked Sudbø to contact professor Kjærheim at the Odontology who is supposed to have advised Sudbø to contact Koppang. According to his statement, Reith did not collect any material from the Odontology. It is somewhat unclear how many patients are involved. Sudbø states that the material was sent in several turns, and comprised patients with leukoplakias as well as erythroplakias. The Commission has not found original copies of cover letters or data lists from the Odontology which can document how many and which patients are involved.

Nor can the Commission see that any participant’s consent or dispensation from the duty of secrecy exist for the delivery of the patient data, although this was a requirement for delivery of patient information subject to secrecy, see section 4.2.4. The delivery thus appears to be contrary to the set of rules enforced at that time. The University of Oslo has not been given the opportunity to comment on this fact, see sections 2.4.6 and 7.3.2.

Hanna S. Koppang, who was responsible for the pathology at the Odontology, cannot remember to have delivered material to Sudbø during the relevant period either. But the Commission can for that reason not conclude that the material was not delivered to Sudbø or Reith, since Koppang’s statement is marked by failing recollection from this period.

Sudbø has asserted that it is surprising that professor Koppang allegedly does not remember to have delivered clinical material to Reith and Sudbø. He has stated that in the offices of Reith and Puntervold there is supposed to be lists sent from professor Koppang which allegedly shall show the number of patients, the number of lesions per patient, grading of dysplasias, transferred to carcinoma in situ as well as the time when these were sent. According to Sudbø, Koppang sent leukoplakias in several turns, then erythroplakias, although in a far smaller number, since these are far more rare than leukoplakias. Sudbø also alleges that he (“we”) has sent the total biopsy specimens from Gade to Koppang for classification/grading of dysplasias, and that lists of this are supposed to exist with Reith or Puntervold. The Commission has submitted this information from Sudbø to Ruth Puntervold and Reith, asking whether they have seen or have had access to files, cover letters and the like which can shed light on what Sudbø has received from the Odontology and Hanna S. Koppang. Puntervold states that she received the blocks with marking of block id., and that this was the basis for the journal L 34 which was established for the preparation of ploidy samples from the Odontology. Apart from this, she has no knowledge of Sudbø’s contact with the Odontology. Reith says that he now cannot find lists,
cover letters or the like. However, it should be noted that Koppang has provided the Commission with access to a list which shows that some patient samples were delivered to Sudbø in 2001. In this respect, the material from the Odontology which allegedly forms the basis for the PhD work, appears as being difficult to check.

However, the letter from Sudbø and Reith to professor Bang at Gade dated February 1st, 1996, states that Sudbø and Reith has from “… Odontology institute for pathology, the University of Oslo, been lent 83 biopsies from 63 individuals, taken in the period 1984-89. About half of these are biopsies sent by dentists from Eastern Norway, Middle Norway and North Norway. The other half is biopsies taken at the Clinic for Oral Surgery and Oral Medicine at the Faculty of Odontology, the University of Oslo …”.

Moreover, Sudbø has stated to the Commission that 63 persons seem to tally. The figure 63 persons from the Odontology seems also to be in accordance with the Commission’s and the Cancer Registry’s own investigations. A list that the Cancer Registry made in 2006 after having themselves obtained and entered personal identification numbers for the patients who had names and dates of birth only, shows 132 observations divided on 62 different persons, which means that 70 of the observations are duplicates.31

Accordingly, the Commission finds that Sudbø originally and basically had access to patient data and material from around 63 different persons from the Odontology in Oslo.

**The Cancer Registry’s linkage**

In order to have the collected patient data checked and supplemented, they were sent to the Cancer Registry for linkage. A letter of February 20, 1996 from Jon Sudbø to Chief Physician Frøydis Langmark at the Cancer Registry states:

> “I refer to our telephone conversation some weeks ago in which we discussed the possibility for a review of the Cancer Registry’s data base as part of a retrospective prognostic study of premalignant changes in the oral mucosa. Regrettably, our data will arrive later than indicated to you. In the meantime, we have collected data relating to persons with the diagnosis oral dysplasia also from Haukeland hospital, and the collection and systematization of these data have taken some time.

> As stated, this takes place at the Department of Pathology, section for image analyses, at the Norwegian Radium Hospital, and I am currently working with a project aiming at defining morphological characteristics at premalignant conditions (dysplasia) in oral mucosa. The study is funded over three years by the Norwegian Cancer Society. Supervisor for the project is Professor Albrecht Reith, MD, Department of Pathology, the Norwegian Radium Hospital.

> Enclosed is a transcript of the relevant patients. This represents a collection of patients from the entire country, diagnosed from 1984 up to 1995. Personal data are given as far as they are known. I also enclose a disk with the relevant data. Could you forward this to the relevant person.”

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31 List: "Oslo_030606.xls"
The annexed list of patients comprises data from 226 patients. The Cancer Registry has referring letters and similar documentation related to the relevant patients. The Cancer Registry’s subsequent investigations in 2006 show that 63 out of 226 persons originated from the Odontology. This number of patients is then in accordance with the number in the aforementioned letter from Sudbø and Reith dated February 1, 1996. The remainder (163 out of 226) originates from Gade’s Institute (see below).

However, the Cancer Registry has pointed out that the persons who subsequently have been proven to originate from the Odontology did not have personal identification numbers, and that they for that reason were not linked. The Cancer Registry is certain that the only patients that were linked and returned to Sudbø were 160 persons, who all originated from Gade (3 persons were excluded, and of these two were duplicates and one had adenoma in the stomach). Thus Sudbø received linked data for 160 patients from the Cancer Registry on March 22, 1996.

Sudbø has maintained that he was not aware that the 63 patients from the Odontology were not linked. On the other hand, Sudbø states that with the help from Reith and a laboratory technician at the Radiumhospitalet, Ruth Puntervold, he got access to the patients’ full personal identification numbers from the Population Registry, and thereby was able to run a link with Cancer Registry data. Puntervold denies that she has assisted Sudbø in this. Also Reith denies that he has helped Sudbø to provide information from the Population Registry or assisted him with linkage. The Commission thus finds it quite unlikely that the patients from the Odontology had person identification numbers and that they were linked with the Cancer Registry data. In light of the information from both Puntervold and the Cancer Registry on this point, the Commission finds no grounds on which to accept Sudbø’s allegations regarding the actual facts.

The cause of death registry has not registered any inquiries from Reith or Sudbø. At that time, Sudbø did not have a clinical position at the Radiumhospitalet, and thus not a free access to the hospital’s case notes. Consequently, the Commission finds it to be not very likely that inadequate sets of data were supplemented in this way.

The Commission thus finds that Sudbø probably had access to human biological material and referring letter information on insufficient patient data (patient data not linked with Cancer Registry data in order to exclude coincidental and previous cancer) from 63 individuals from the Odontology. This means that all the patients from the Odontology ought to have been excluded from the study initially, and that the original number of patients should have been 63 persons less than what was stated in the dissertation and Oncology 2001.

Sudbø’s assertions that the Commission is wrong on this point must be rejected, since the Commission does not find it likely that these 63 persons were linked with Cancer Registry data as alleged by Sudbø. It is also a fact that the so-called Sudbø8 file which formed the basis for New England Journal of Medicine 2004 (and thus in all essentials also New England Journal of Medicine 2001), did not comprise any persons from the material from the Odontology.
The linkage of patient data with Cancer Registry data for research purposes presupposed then, as now, that a participant consent or dispensation from the duty of secrecy existed, see section 4.2.4 and the Cancer Registry’s framework licence dated December 9, 1985, cf item 4.3 of the licence. This was not so.

The Cancer Registry was notified that the Commission was considering expressing a certain criticism on this basis, and made use of its right to comment on an earlier draft report, section 7.3.4. In a letter to the Commission of June 2, 2006, the Cancer Registry submitted that the criticism in the draft is based on an erroneous perception of the Cancer Registry’s different roles. The Cancer Registry alleges that they understood Jon Sudbø’s request of February 20, 1996 as a routine request for follow-up data for patients at the Radiumhospitalet, Department of Pathology. The Cancer Registry alleges that delivery of the required data did not take place as “data supplier or partner in a research project, but as part of the registry role relating to the safeguarding of data completeness and follow-up of patients”, focusing on the central problems which normally are involved in such a follow-up. It is alleged that the data exchange that takes place between the individual hospital and its departments and the Cancer Registry in relation to quality assurance, entails that the Cancer Registry contributes to the diagnosis and treatment departments’ quality control of “their” patient material, at the same time as this normally leads to a quality increase of the Cancer Registry’s main data base. The Cancer Registry alleges that this mutual quality control is “… a most central part of our registry function”, and that this “activity has been ongoing on a routine basis for all years, and that it is considered to be covered by the previous licence as well as the current regulations”.

Further, the Cancer Registry submitted that the draft criticism seems to be based on the assumption that the Cancer Registry should have understood that Sudbø applied for data for a research project. If so, this is a basis for criticism that the Cancer Registry considers to be unreasonable. The Cancer Registry in this connection refers to the fact that Sudbø’s approach was accompanied by a detailed list of patients, that the cover letter stated that Sudbø’s project took place at the Radiumhospitalet, Department of Pathology, and that data had also been obtained from Haukeland Hospital. The Cancer Registry submits that in light of all facts relating to Sudbø’s approach in 1996 there was no reason to believe anything else than that the patient list concerned the Radiumhospitalet’s own and called-in biopsy preparations, and that the request was made as a request for follow-up data – a type of requests that the Cancer Registry receives and deals with continuously. It was not until 2006, when this case had come to light, that the Cancer Registry realized that the material which Sudbø in the request from 1996 wished to have quality-assured, did not concern the Radiumhospitalet patients, but material from Gade’s Institute and the Institute of Odontology’s department of pathology. The
Cancer Registry furthermore submits that if the facts had been correctly stated in 1996 Sudbø would not have been given Cancer Registry data. The Cancer Registry in this connection refers to the fact that Sudbø’s request in 1994 was refused exactly because he wanted follow-up on other institutions’ patient material, and also wanted personal access to the Cancer Registry’s data base.

The Commission has considered the remarks made by the Cancer Registry and compared them with the information provided in Jon Sudbø’s letter of February 20, 1996 to the Cancer Registry, quoted above, and other information. On that basis, the Commission finds that it appears from the letter that it is a question of a research project, something which the Cancer Registry ought to have understood. The handing over of the data thus appears to be contrary to the licence conditions, see otherwise section 7.3.4.

The material from Gade

In the aforementioned letter of February 1, 1996 from Sudbø and Reith to professor Bang of Gade, it is further stated:

“… We also have an agreement with chief physician Langmark at the Cancer Registry relating to obtaining data regarding which of these persons later developed oral cancer. However, our existing material of 63 individuals is too small to be able to be used in such a retrospective study and our question to you is therefore whether you could place a corresponding material at our temporary disposition. To begin with, we are interested in personal data from individuals who have been given the diagnosis of mild, moderate or severe squamous epithelium dysplasia from the oral cavity, regardless of localization. If data from the Cancer Registry should show that the percentage that has developed oral cancer is sufficiently large, it would also be of interest to borrow the biopsies for the production of biopsy specimens for coloring and examination.”

A data list with patient data for the period 1981-95 was sent in an undated letter from Bang to Reith and Sudbø. The Commission cannot see that any participant consent or dispensation from the duty of secrecy for the delivery of patient data exist, although this was a requirement when patient information subject to secrecy was to be delivered, see section 4.2.4. Thus, the handing over of the data appears to be contrary to the set of rules applicable at the time, see also section 7.3.3. The University of Bergen has not commented on the Commission’s draft criticism. A letter dated May 15, 1996 from Reith to professor Andreas Myking at Gade (to whom Bang had referred Reith), states:

“We have at our department been in contact with professor Gisle Bang of Haukeland Hospital. He has sent us data from 161 patients diagnosed with dysplasia from mucosa (see the annexed list). We have compared these data with information from the Cancer Registry. It appears from these data that approximately 50% (79/161) of the patients with the diagnosis mild, moderate or severe mucosa dysplasia within a five years’ period
developed squamous cell carcinoma of the oral cavity … Our question to you is therefore whether it is possible to be sent **cut blocks and copies of referring letters** from the patients in the lists we have enclosed …”

Sudbø and Reith were sent referring letters from Gade, a fact that is confirmed in, i.a., a letter dated December 9, 1996 from Sudbø to Professor Anne Christine Johannesen at Gade. The Gade material originates from clinics spread all over Western Norway.

The patient number of 161 persons is confirmed by the Cancer Registry, which in February 1996 linked 161 persons with the Cancer Registry’s data. (Two out of 163 were duplicates. One more person was according to the Cancer Registry furthermore excluded because of adenoma in the stomach.) Consequently, the list which Sudbø and Reith got from the Cancer Registry comprised linked data from 160 or 161 persons. The Cancer Registry’s investigation in 2006 shows that all 161 persons who were linked originated from Gade.

The aforementioned letter dated December 9, 1996 from Sudbø to Johannesen states:

“Enclosed please find a set of copies of referring letters I have received from Professor Gisle Bang, relating to dysplasia from the oral cavity. You will also find enclosed a Microsoft Excel spreadsheet stating patient data as they are linked from referring letters to data from the Cancer Registry. What is particularly striking with the material, is the high share of dysplasia showing malignant transformation (50%). It therefore seems to be necessary to have verified the original diagnosis (mild, moderate or severe dysplasia) and exclude any CIS. You have been in contact with Professor Albrecht Reith regarding this material, and you probably know the problem from this. Thank you for your interest and will to assist in this!”

The letter of reply from Johannesen to Jon Sudbø dated May 21st, 1997 states:

“… I have looked at all the biopsy specimens from the pile I was sent. I have a series of comments which I shall try to express as clearly and briefly as possible:

- I have tried to make a list of names, P-numbers (biopsy number) and diagnosis. All this is in normal type.
- My objections are in italics.
- Some referring letters are lacking in relation to the list received. These are mentioned by name (italics) without any further text.
- At many places there is no correspondence between the diagnosis on the list received and the biopsy answer! Here biopsy answer must of course apply.
- The explanation of why the material from Bergen has such a high frequency of malignant transformation is that you have perhaps not compared the time of their dysplasia diagnosis with the time of the malignant diagnosis. For example, at several places it appears that dysplasia diagnosis lies in a resection border in a carcinoma that has already occurred. This is therefore no
malignant transformation but a dysplasia that has already had a cancer diagnosis. Several of the patients have also previously been operated for squamous cell carcinoma.

- As regards the diagnoses, I have not changed many. I have accepted a deviation of 1 degree (mild-moderate, moderate-serious) without having corrected the diagnosis, this because the grading to such a relatively large extent is subject to personal assessment. Where there are obvious errors or major deviations, I have corrected the diagnosis.

I hope this is sufficiently clear. Then I want to wish you good luck with your further work!”

It is to be noted that Johannesen’s list comprises data from 144 different persons only. Reith thinks the letter from Johannesen looks “straightforward”, but he wonders why the Cancer Registry only excluded two persons out of 163, whereas Johannesen apparently excluded a further 17 persons. Reith states that he cannot recall having seen/read the letter before.

The Commission asked itself the same question. The probable explanation is that the list of 163 observations, which originated from Gade, and which were linked by the Cancer Registry in the beginning of 1996, comprised two duplicates, so that the list comprised 161 persons after linkage. In a list recently prepared by the Cancer Registry there is a column called “Diagnosis on A.C. Johannesen’s quality assurance list”. This column contains 17 blank observations (which also are persons). This probably means that Johannesen has quality assured the diagnosis of 161-17=144 persons. This agrees with the figures the Commission’s own investigations have produced, i.a. through comparisons with block numbers, see below. This is also consistent with what Johannesen wrote in a letter of May 21, 1997: “There are some referring letters that are missing in relation to the list sent. These are mentioned by names (italics) without any further text.”

Total number of patients: This means that Sudbø and Reith in the summer 1997 were left with a reclassified data file from Gade’s Institute which was linked with the Cancer Registry data, with data from only 144 persons, i.e. 119 persons less than what is stated in the dissertation and Oncology 2001.

The Commission finds it surprising that in the communication with Gade, after the linkage with the Cancer Registry data, there is no reference to the material from the Odontology. If the 63 persons from the Odontology, which the Cancer Registry has not linked, and which for that reason should have been excluded, nevertheless are added, the data material in the best case consists of data from 144+63=207 different persons.

It should be noted that the number of samples (tissue blocks, biopsy specimens, etc) far exceeds this number, because there are several samples from the same person, something which is totally usual.

Sudbø has expressed that he has no qualification to comment on these figures, stating that it was Reith who was responsible for the handling of data files between Gade’s Institute and the Cancer Registry. However, the letter from Johannesen was addressed to Sudbø alone, although Reith does not exclude in his

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32 Memo from the Cancer Registry of March 7, 2006 with annexes.
statement to the Commission that he has seen the letter dated May 21, 1997. He further states that “the diagnoses contain so many histopathological terms unknown to me that I would have discussed them with a pathologist at the department, I know I have never done that.” Reith has otherwise referred to a memo written by Sudbø in 2000, in which Sudbø consistently uses the “I” form in his description of the handling of the data material. In light of this, the Commission cannot trust Sudbø’s assertions relating to Reith’s alleged central role in the handling of data files, see also the letter of February 20, 1996 from Sudbø to the Cancer Registry, rendered above, and the letter from the Cancer Registry to Jon Sudbø of March 22, 1996.

The Commission has considered whether Sudbø and/or Reith may have misunderstood and mixed up the number of samples with the number of patients, etc. The Commission finds this not very likely. The Commission here finds reason to refer to Johannesen’s letter of May 21, 1997, which in the Commission’s opinion should not give room for misunderstandings and misinterpretations. In any case, the letter should have caused a thorough reevaluation on their part which could have brought any misunderstandings to light.

The Commission has furthermore questioned whether the material from Gade and, as the case may be, the Odontology has subsequently been supplemented, for example by material from other patients having been collected and brought into the project, for example from Gade, the Odontology, private practices or other channels. The Commission has not found any grounds at all for this being the case. The Cancer Registry drew the same conclusion. This is in fact confirmed also in the dissertation and in the articles. Such a supplement is also contrary to expectations for more practical reasons.

Sudbø’s allegations that he obtained supplementing information as regards complete personal numbers do not, in the light of Puntervold’s, Reith’s and the Cancer Registry’s statements, appear as probable, and they are also somewhat surprising and contradictory in light of his other allegations that it was Reith who was responsible for the handling of data files between Gade and the Cancer Registry and the arrangement of the data material otherwise. On this background the Commission maintains its clear understanding that the patient number stated is not correct.

Accordingly, the Commission finds that there was probably no access to linked data from more than 144 persons, in the best case from 207 persons.

Exclusion of patients with erythroplakias (red patches in the oral cavity)

In the PhD dissertation is stated that 21 out of 263 patients were excluded initially from analyses of survival because they had erythroplakias. Erythroplakias is far more serious than white patches, and also occurs much more seldom. It should be noted that these persons, i.e. persons with erythroplakias, probably were
included in a subsequent study with 37 erythroplakia patients which formed the basis for a scientific publication.\textsuperscript{33}

The Commission finds that the figure 263 cannot be correct. Whether there were 21 persons with erythroplakia in the basic material seems uncertain to the Commission. Johannesen of Gade, however, has stated that erythroplakia were not registered at Gade. If so, this means that patients with erythroplakia must originate from the Odontology. And Sudbø himself stated to the Commission that the erythroplakia originated exclusively from the Odontology. The Commission is in some doubt that 21 of the 61 persons who came from the Odontology had erythroplakia, but this can nevertheless not be excluded due to the missing documentation of these patients. The article that reported the follow-up results from 37 erythroplakia patients does not state from where the patient material (which allegedly was collected in 1988-2000) originates.

However, Sudbø has later on, in comments to the preliminary draft investigation report, maintained that the erythroplakia originate from the Odontology. He has stated that a relatively large material of erythroplakia existed there, because Hanna S. Koppang for many years had taken an interest in these lesions. Sudbø has stated that “the original 21 erythroplakias, originally submitted as leukoplakia, but classified as erythroplakia because they originally had been described as erythroleukoplakia.” As mentioned, the Commission is in some doubt about this explanation. In addition, the Commission has reviewed the list of the 63 persons coming from Oslo, without finding any references to diagnoses of erythroplakia.

Even if the Commission does not manage to document that 21 persons did not have red patches in their oral cavity as stated in the dissertation, there is nevertheless such considerable doubt and uncertainty related to this material that it gives reason to concern for whether it is correct at all. This particularly applies in light of other findings in this case, which will be accounted for below.

\textit{Classification and reclassification of patients with white patches in their oral cavity – the inclusion and exclusion process}

In figure 1 in New England Journal of Medicine 2001 and figure 5 in the dissertation (see figure 1 in the report) is stated that 242 patients with white patches in their oral cavity (leukoplakia), originally were included in the study after the alleged exclusion of 21 persons with red patches in their oral cavity (erythroplakias).

The Commission refers to the account above in which is determined that it is not likely that this figure is correct, i.e. that one has not had access to 242 persons with dysplasia diagnosis. The real figure is

144 or in the best case 207. The Commission nevertheless finds reason to discuss the actual facts which are alleged by Sudbø et al. in the dissertation and articles.

The key item at this stage of the study was to decide which patients met the criteria (the inclusion criteria) to be made part of the planned ploidy study, i.e. a so-called inclusion process. Before starting a research process, it is usual to state inclusion and exclusion criteria for the research participants, i.e. which patients have the qualities to be studied, and which have qualities that mean that these persons cannot be included in the study. It is important that this inclusion process takes place according to certain criteria determined beforehand and that can be checked, in order to avoid inappropriate selection.

To find which patients with dysplasia diagnosis met the inclusion criteria, the patients were checked against three key criteria (see figure 1):

1. Dysplasia classification: One tissue block from each individual patient had to be classified to see which type of dysplasia the individual patient had. The patients were then to be divided according to the criteria mild, medium and serious dysplasia.
2. Prior or simultaneous cancer diagnosis: Patients who had or had had oral cancer were to be excluded. This was because it was change/transformation from white patches to cancer over a certain time interval which was to be studied.
3. Insufficient data material: Persons for whom sufficient data were not available had to be excluded.

1) Dysplasia classification (the reclassification): It appears from the three articles and subsequent articles that the classification was made by four pathologists who reclassified tissue samples from each individual patient, according to guidelines prepared by the World Health Organization (WHO). New England Journal of Medicine 2001 page 1270 states for example: “All histological sections were subsequently reevaluated by four pathologists according to the guidelines of the World Health Organization.” According to how the procedure is described, it must be understood that the reclassification took place blindly (without knowing the patients’ identity, diagnoses and the like), and that the pathologists worked independently of one another. This is because the classification was based on assessment, and because it was a key element in this study that the classification became as correct as possible.

It is therefore correct, as is stated in the articles and the dissertation, that patients in relation to whom one disagreed on the diagnosis grading, had to be excluded. In the articles and the dissertation is stated that altogether 46 patients had to be excluded for this reason. In Oncology 2001 the figure is 45 (see figure 1), but this is explained in the dissertation by an “outlier” having been excluded, but the Commission cannot see that anything was mentioned about this in the article. Sudbø states that it was deleted by the editor.
This reclassification process is described in detail in J Pathol 2001, in which one also directly compared the classifications of the individual pathologist.

It is a fact that the four pathologists referred to are

- Gisle Bang, Gade’s Institute
- Hanna Strøm Koppang, the Odontology
- Anne Christine Johannesen, Gade’s Institute
- Bjørn Risberg, the Radiumhospitalet

This appears explicitly from Oncology 2001 in which these four persons are listed with names in acknowledgements. There is no doubt that all of them are qualified pathologists. It is also a fact that the original dysplasia classifications in no way were so sure that they could be used in the inclusion process. This means that originally all patients had received a dysplasia diagnosis, but Gade and the Odontology were and are very clear that the grading was flawed and not directly applicable for scientific purposes. In other words, there was an obvious need for a blinded reclassification for scientific purposes. This need was at an early stage in fact underlined explicitly to Jon Sudbø by the department manager, Professor Jahn Nesland, who is a pathologist himself. Nesland states to the Commission that such a reclassification for scientific purposes normally is performed blindly with two independent pathologists who afterwards have a so-called consensus meeting to compare results in order to arrive at an agreed dysplasia classification. Thus, it is a fact that it was a question of reclassification of the entire material these four were to make. One may ask why one allegedly used four pathologists instead of the customary two. A possible answer is that the classification becomes more certain the more independent pathologists are used for classification.

However, the Commission cannot see that the information that the reclassification was made by four pathologists is correct. Admittedly, Gisle Bang was central in the collection of the original material. Nevertheless, it is a fact that Gisle Bang did not make a reclassification of all the material. In the best case, he can be deemed to have participated in the original, but for scientific purposes obviously flawed classification of parts of the material from Gade, but not by far the whole material.

The same applies to Hanna Strøm Koppang. Admittedly, Koppang was central at the collection of the original material, but she has hardly participated in the reclassification of the material. In the best case she can be deemed to have contributed to the original, but for scientific purposes obviously flawed classification of the material from the Odontology, but not by far the whole material.
Anne Christine Johannesen has in a sense participated in a reclassification of material from Gade, i.e. 144 of the patients. However, she has not classified the material from “all” the patients. But Anne Christine Johannesen is unable to understand that she is supposed to have participated in a reclassification also of the Gade material. She states to the Commission that it was a fact that her task was to quality-assure the material they had delivered to Sudbø and Reith, such that her responsibility was limited to doing so. She believes this appears clearly from the aforementioned cover letter dated May 21, 1997 to Jon Sudbø with a copy to Reith. In Johannesen’s letter reference is made i.a. to a letter from Reith to Myking of May 15, 1996, in which as mentioned reference is made to the fact that the linkage with the Cancer Registry data had identified a transformation rate from dysplasia (white patches in the oral cavity) to cancer of as much as 50%. This sensational finding is also emphasized by Sudbø in a letter to Anne Christine Johannesen of December 9, 1996. However, Johannesen points out that the high transformation rate of 50% which Sudbø and Reith had referred to, is based on several obvious errors, for example that those that had received dysplasia diagnosis had a prior or simultaneous cancer diagnosis, such that no transformation can be determined. It further appears that Johannesen did not make a careful reclassification based on the criteria mild, moderate and severe dysplasia.

In this context it should also be noted that the Cancer Registry this year has found it very difficult to comprehend why Sudbø and Reith in December 1996, several months after the Cancer Registry’s linkage, asked Johannesen to revise/reclassify diagnoses relating to patients who should have been excluded based on the information they had received from the Cancer Registry, and based on far more data per patient than Johannesen had any possibility to possess.34

Nor did Bjørn Risberg see himself as one of the four pathologists. Risberg states to the Commission that when he read this section in the article, he assumed that this concerned four pathologists which were unknown to him, and that his task had only been to quality-assure the reclassification performed by others. Risberg cannot recall how many samples he classified, i.e. that he may have classified between 150 and 242 samples. The Commission finds it surprising that Risberg has not been informed that he was one of the four pathologists. In the dissertation it is only Risberg who is thanked for having made a reclassification, whereas Koppang is thanked for histological classification.

In his comments to the preliminary draft investigation report, Sudbø writes among other things that he is “entirely incapable of understanding that the original dysplasia classifications could not be used for scientific purposes. This is the first time that I have heard that this point has been raised. However, it was discussed whether one should have had consensus meetings and calibration by pathologists prior to the classification. I objected strongly to this, because the clinics base their treatment on routine diagnostics, not especially constructed diagnostic procedures and assumptions. Everyone involved in this project,

34 Letter from the Cancer Registry to the Commission of May 9, 2006.
including Reith, Bryne and A.C. Johannesen, agreed that there was much to say for this view.” Furthermore, Sudbø asserts that the term “reclassification” was consistently used only to designate that different pathologists, independent of one another, had classified and graded the dysplasias.

The Commission does not have confidence in Sudbø’s explanation on this point, since in the articles and the dissertation he so clearly and unambiguously refers to a “reclassification” by four pathologists in line with the WHO’s guidelines. It is also a fact that Johannesen was not “involved in the process” by discussing the planning and the challenges as the impression seems to be by Sudbø’s explanation.

*The Commission finds that the reclassification was not performed by four pathologists in the manner described in a series of articles and the PhD dissertation.*

In the articles and the dissertation it is alleged that 46 patients were excluded because one did not obtain consensus on the grading of the dysplasia diagnosis. There can hardly have been any consensus meeting or the like, when in the best case it is only one pathologist who classified the entire material. None of the four stated pathologists have been participating in any consensus meeting or the like. Sudbø states that there was no consensus meeting between these pathologists, but that there was consensus in the form of “conformity of opinions”. The Commission also finds such conformity of opinions to be entirely unlikely, as long as the total material hardly was assessed by four pathologists.

*The allegation that 46 patients were excluded due to failing agreement among four pathologists regarding dysplasia grading thus appears as unfounded and erroneous.*

The Commission has not found anything to underpin that the figure 46 is correct. The Commission has no alternative figure to put forward, however, as long as the material has not been reclassified in a proper manner for scientific purposes, and as long as the Commission believes that the patient basis was far smaller than what is stated.

2) Preceding or simultaneous cancer diagnosis: The articles and the dissertation state that 36 patients were excluded from the study because they had a simultaneous or preceding cancer diagnosis. The point of the study was exactly to study which patients, after having received a dysplasia diagnosis, *at a later point in time* received a cancer diagnosis. Consequently, persons who had a simultaneous or preceding cancer had to be excluded. The Commission’s review of available data files shows, however, that the number of patients with a simultaneous or preceding cancer diagnosis must have been far higher than what is stated in the articles and the dissertation. Reference is again made to Johannesen’s letter of May 21, 1997 to Sudbø and Reith in which precisely this point is emphasized, i.e. that a far higher number of patients had a preceding or simultaneous cancer diagnosis, and that this was something Sudbø and Reith obviously had overlooked.
Johannesen’s data file annexed to the aforementioned letter shows that at least 47 out of 144 persons should have been excluded for this reason. The Cancer Registry’s own investigations also conclude that this figure should be far higher. The Cancer Registry believes that at least 12 out of 63 persons from the Odontology and 76 out of 156 persons from Gade ought to have been excluded for this reason.

Sudbø states that this information is new to him, and he is not quite able to comprehend it. He raises the question of whether all preceding or simultaneous cancer diagnoses are referring to oral cancer or related (tobacco-conditional) cancer. He points out that it is of limited interest whether a patient has had colorectal cancer, cervical cancer, or melanoma prior to oral cancer. Finally, he raises the question of whether an updating of the Cancer Registry’s data base has taken place as regards registered cancer incidents since 1995/96.

The Commission here refers to the letter from Johannesen that shows that already in 1996/97 one was aware of all cases of preceding or simultaneous cancer. For the avoidance of doubt, the Commission has in addition compared the Cancer Registry’s list from 1996 with the Cancer Registry’s data from this year. For the most part there is consistence both as regards cancer dates and localization (the type of cancer diagnosis). There are a few deviations regarding the referring letter date, but nothing of substantial importance. Thereby, it is also clear that this concerns preceding or simultaneous oral cancer, and not other types of cancer. In this context, the Commission has checked the localization code entered for each patient to see if the latter is the case.

Accordingly, the Commission finds that the number of persons with preceding or simultaneous cancer diagnosis was far higher than the number stated in the articles and the dissertation. This is a very serious matter, which clearly and isolated seen entails that the research results cannot be considered as valid.

3) Flawed data material: Finally, in figure 1 is stated that 10 patients were excluded because one did not have appropriate data or material from these patients. Based on the discussions above, this number must be considered as being unlikely low. Reference is here made to the fact that the material from the Odontology (63 patients) was not linked by the Cancer Registry, and therefore should have been excluded for that reason, if not before. Reference is also made to the fact that one only had material from 144 patients from Gade.

It is obvious that far more patients should have been excluded because one did not have sufficient material to include them in the study.

In this context, the Commission finds reason to point out that Johannesen in a letter of May 21, 1997 remarks that “there is no conformity between the original diagnosis and biopsy answer and that the latter must apply”. Furthermore, it is remarkable that Jon Sudbø in an email to Johannesen of December 11, 2001 writes that “The dysplastic material is unadulterated in the sense that it does not include patients with

35 List: "Sammenlign_kreft96_og_06xls" ["Comparison cancer96 and 06xls"]
simultaneous or preceding carcinoma, neither in their oral cavity or UADT otherwise. The not dysplastic material is restricted, 46 cases.”

Based on this, the Commission finds that there are so many important errors and flaws in the inclusion and reclassification process that the resulting outcome is not credible. The Commission is of the opinion that the errors in the reporting are serious.

The inclusion of 150 patients in the ploidy study

According to the articles and the dissertation, altogether 150 patients were included in the study itself. This ploidy study, which is the experiment proper in the PhD project, was made in 1998-99.

At that time Sudbø had used up his four years as a research fellow, and also a last supplementary year. He was then left without any fellowship salary. His closest superior, Professor Håvard Danielsen, PhD, then proposed that Sudbø should use the method developed by Danielsen to analyze the material that Sudbø had in his possession. Sudbø accepted this, and Danielsen arranged for six months of salary funds from the Radiumhospitalet as well as the assistance of a laboratory technician. Sudbø alleges that he himself had taken the initiative to this image analysis already in 1998, but had not got access to the equipment because his oral cavity project was not a prioritized project at the department.

Although it is unlikely, based on the preceding discussions that there were 150 patients that met the inclusion criteria, the Commission has nevertheless found reason to investigate the ploidy analysis in more detail. This is of importance for the clarification of whether the obvious errors that so far have been discovered are due to sloppiness and incompetence or scientific dishonesty.

The Cancer Registry’s investigation: In its investigation, the Cancer Registry refers to Johannesen’s “limited reclassification” showing that one was left with a maximum of 85 patients only who met the inclusion criteria, divided on mild dysplasia (58), moderate dysplasia (18) and severe dysplasia (9). (In addition, 8 persons were given the diagnosis dysplasia, 4 hyperplasia, 4 preceding cancer, 43 simultaneous cancer – in aggregate 144). Correspondingly, table 1 in New England Journal of Medicine 2001 shows a distribution on mild dysplasia (49), moderate dysplasia (57) and severe dysplasia (44) – in aggregate 150. In other words, the numbers stated in the article do not at all correspond with Johannesen’s classification. Nor does the grading stated in the New England Journal of Medicine 2001 correspond to the list Jon Sudbø according to the Cancer Registry received from the Cancer Registry in 1996, and which had the following division: dysplasia 4, mild 38, moderate 22 and severe 99, in aggregate 163.

The Cancer Registry believes that this number of patients that could be included could have been 79 as a maximum, particularly because of preceding or simultaneous cancer diagnosis (77 out of 156). That is to say close to half of what is stated in the articles and the dissertation.
In spite of the unambiguous findings of the Cancer Registry, based on its own investigations and Johannesen’s independent classification, the Commission has nevertheless found reason to make some investigations of its own. This is connected with the fact that the Cancer Registry’s conclusion that no doubt manipulation and fabrication of data was involved, was quite sensational and serious.

The Commission’s own investigations of patient lists and the ploidy analyses: The Commission has been given access to several lists which apparently contain data from 150 patients who probably were included and studied in the ploidy analysis which took place in 1999. It is a fact that the lists comprise 150 observations, i.e. registrations. It is also probable that someone (see in more detail about this below) has analyzed at least 150 blocks/samples/preparations/monolayers. Based on the aforementioned investigations and findings, the Commission raised two entirely central and specific questions:

1. Was the ploidy analysis performed on 150 different persons, or may it be that several analyses originate from the same person?
2. Do the persons included and studied really meet the inclusion criteria?

With the help of available data lists and comparisons between them, and comparisons with among other things data from the Cancer Registry, it has been possible to obtain precise documentation of which patients were actually included, including these patients’ disease history (i.e. whether they met the inclusion criteria).

The lists and the patients form the basis for the three mentioned articles, the dissertation and several subsequent publications, i.a. New England Journal of Medicine 2004, and have therefore been in the very center of attention for the Commission, see annex 3.

The Commission will here discuss these lists in more detail. In particular three lists are of interest:

- **L-29.** This list is assumed to be the original list used in the study, and which the Commission has received from Danielsen. As head of section, Danielsen obtained it from the archives in 2006 on the Commission’s request. It is noted on the list that it was produced in April 1998. The list is assumed to form the basis for the PhD project, including New England Journal of Medicine 2001.

- **Rawdata.** The Commission has received this list from Reith. Reith has stated that he had not seen this list until 2006, when he asked Ruth Puntervold for it in connection with this case. Puntervold is supposed to have received the list from Sudbø in 2005 in connection with Bjørn Risberg’s wish to measure the preparations again, see 5.3. It is in harmony with, and is probably based on, L-29. According to Reith, the data list forms the basis for New England Journal of Medicine 2004, which again in all essentials is based on New England Journal of Medicine 2001.
• **Sudbø8.** The Commission has received this list from J. Jack Lee at MD Anderson, who again received it from Sudbø. Lee is the bio statistician who ran the analyses which form the basis for New England Journal of Medicine 2004. According to Lee, this list is the basis for New England Journal of Medicine 2004.

These three lists are in harmony with each other, which means that there is a preponderance of probability that they originate from the same patient material. However, the individual lists contain more or other registrations. The Commission has not found any basis for these lists not forming the basis for the analyses which again form the basis for the publications in i.a. New England Journal of Medicine 2001 and 2004. Nor has Sudbø or others submitted any patient lists that deviate essentially from these lists.

The rawdata list comprises preparation/block/sample numbers which make it possible to obtain information from the Cancer Registry. This list is, apart from block numbers, identical to Sudbø8.

The table in annex 4 shows the 150 observations (records) which the Commission has assumed formed the basis for the article in New England Journal of Medicine 2004. The first column is a continuous numbering of observations as listed in Rawdata and Sudbø8. The second column comprises unique persons. Each observation in Sudbø8 comprises one or several preparation numbers (block numbers). These preparation numbers were linked to the same person apart from two members in observation 51, which proved to belong to two different persons. This observation is therefore listed twice. The third column is the preparation number itself. This is blanked out for reason of personal data protection. There were 8 observations on the rawdata file for which there were no preparation number. For these 8 “missing” is noted in the column. Then follows a column showing the year when the preparation (the sample/biopsy) was taken. The three next columns are from the file which the Cancer Registry delivered to Sudbø in 1996. Then follow three columns from Sudbø8. The column “year leukoplakia” should be corresponding to the column “year preparation”. Finally there is a column showing whether preparations for ploidy classification had been made.

The Commission has had access to dates for leukoplakia diagnoses and dates for cancer. These coincide entirely with Rawdata and Sudbø8. Moreover, it should be mentioned that information on age and tobacco is entirely in conformity on the two files. This documents that these two files must originate from the same patient basis.

This comparison also documents which persons did not meet the inclusion criteria, since the date of oral cancer is before the sample (block/preparation number) was taken. The Commission shows that 69 of 150 observations should have been excluded for this reason. The comparison further documents that there are only 64 different persons on the list which we could document as not being contrary to the inclusion criterion. It should be noted that the year has been removed from the block number in the rawdata list. An indication of
the year could have contributed to someone having discovered the latter error. On the other hand, the year is stated on L29, without anyone having discovered discrepancies with the inclusion criterion.

The comparison shows that none of the dates in Sudbø8 agrees with the data from the Cancer Registry. This means that the dates in Sudbø8 are fictitious. The Commission’s comparison of the Cancer Registry’s list from 1996 and the Cancer Registry’s list from 2006 are in all essentials concurrent, so that an error at the Cancer Registry is excluded. And the Cancer Registry has also made a thorough investigation of i.a. all relevant referring letters, etc.

Totally there is reference to ploidy preparations for 69 out of 150 observations (65 different persons) in the rawdata list. Observation number 51 in the rawdata (patnid_re=51) is listed twice since this observation in rawdata had two preparation numbers which proved to be two persons.

The Commission’s comparison shows the following:

• The rawdata list and Sudbø8 comprise 150 observations made up of a maximum of 140 persons
• Of those 150 observations only maximum 81 observations meet the inclusion criterion
• Of the 150 observations there are only 69 observations in which there is a reference to a ploidy preparation
• Of the 150 observations there are 23 observations in which the year of death is prior to the year of leukoplakia (the year in dateopl). This means that the patient was dead before the diagnosis allegedly was made.
• No observations with block numbers originate from the Odontology in Oslo.

The list “All original blocks and HE biopsy specimens linked to ploidprep and L29 series” moreover shows a connection between block numbers and list numbers (L31 etc) for the observations in which there is a ploidy preparation (probably ploidy classification). In all there are 167 observations. The Commission has a list with a variable/column, “place”, which shows whether the block is from Gade or from the Odontology.36 This is defined based on block number or list number. As regards the list L47 there is verification with block numbers. The Commission’s list shows the following:

<table>
<thead>
<tr>
<th>Observations</th>
<th>Unique block numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing</td>
<td>4</td>
</tr>
<tr>
<td>Gade</td>
<td>97</td>
</tr>
<tr>
<td>The Odontology</td>
<td>66</td>
</tr>
<tr>
<td>In total</td>
<td>167</td>
</tr>
</tbody>
</table>

36 List: "Alle_ploidi_060606.xls" ["All ploidy 060606.xls"]
Consequently, there are 167 ploidy preparations, of which 126 only are unique block numbers. This means that there are unique and thus valid ploidy preparations for a maximum of 126 persons. This can be compared with that, according to Sudbø himself, 196 persons were processed statistically where ploidy classification existed in J Pathol 2001. In other words, this statement hardly agrees with the actual facts.

It is worth noting that only 69 out of 167 ploidy numbers can be linked to L29/Rawdata/Subø8. This means that a ploidy analysis has only been made on 69 (and not 150) of the block numbers existing in the rawdata list, which is the basis for the New England Journal of Medicine 2004.

For this reason, the Commission has seen no point in making a new ploidy analysis of the raw data, since the raw data is so obviously flawed.

Sudbø has reacted to this, and has among other things referred to one of the persons who classified remembering to have received about 150 blocks. Danielsen also believes to have seen a tray with approximately 150 blocks. The Commission would remark to this that one has probably classified approximately 150 blocks, such that those who classified, i.a. Wanja Kildal, probably believed that it concerned the number of persons stated in the articles. But the fact is that it involved many duplicates and many persons who should have been excluded, i.a. due to preceding and simultaneous cancer diagnosis.

The Commission has calculated an age distribution from the file Sudbø8 (which form the basis for New England Journal of Medicine 2004) and compared this with the age distribution for the original data from Gade and the Odontology. For Gade two schedules have been made: 1) Based on a list produced by A.C. Johannesen, which via block numbers is linked with Cancer Registry data, and 2) Based on the file that the Cancer Registry delivered to Sudbø in 1996. Table 2 shows the result for three age groups. Age for Gade and the Odontology is age when the biopsy was taken. Age in Sudbø8 is not defined in more detail on the file itself, but in an email to J. Jack Lee of MD Anderson (who made the analyses) Sudbø writes that this is age at “time at initial diagnosis”. Thus we can assume that there are the same age definitions in the files when age for diagnosis is stipulated as age when the biopsy was taken. Moreover, it is difficult to see which other age it could be in Sudbø8. The table shows that there are far more persons in the age group 65-78 in Sudbø8 than in the other files, also when they are joined. Thus there is a distinct discrepancy between the file which forms the basis for New England Journal of Medicine 2004 and the files which form the basis for this.
Table 2: Age distribution in data file for New England Journal of Medicine 2004 (Sudbø8) compared with the age distribution in data file delivered from the Cancer Registry in 1996 (the Oslo Odontology [62 persons] and Gade [163 persons] and lists from Gade [142 persons].

<table>
<thead>
<tr>
<th>Basis</th>
<th>Canc.Reg.06</th>
<th>Canc.Reg.96</th>
<th>(Canc.Reg.06/ Gade list 98)</th>
<th>JYL06</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oslo</td>
<td>Gade1</td>
<td>Gade2</td>
<td>Oslo+Gade1</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-64</td>
<td>40</td>
<td>79</td>
<td>68</td>
<td>108</td>
</tr>
<tr>
<td>65-78</td>
<td>13</td>
<td>59</td>
<td>53</td>
<td>66</td>
</tr>
<tr>
<td>79-95</td>
<td>4</td>
<td>25</td>
<td>19</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>163</td>
<td>140</td>
<td>197</td>
</tr>
<tr>
<td>Lacking</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>163</td>
<td>142</td>
<td>204</td>
</tr>
<tr>
<td>Average age</td>
<td>56.8</td>
<td>63.5</td>
<td>63.3</td>
<td>61.4</td>
</tr>
</tbody>
</table>

New England Journal of Medicine 2001

New England Journal of Medicine 2004

*Age for Oslo and Gade: Referring letter year minus year of birth; Age for Sudbo8: age in file
The Commission has also had access to the first file which was sent to the USA for New England Journal of Medicine 2004 and compared this with the last file. Table 3 renders the results for some observations.

Table 3. The last 28 records from the first and last file which formed the basis for the article in NEJM 2004.

Both files contain 150 records (lines) numbered continuously at patnid from 1 to 150.

<table>
<thead>
<tr>
<th>Updated rawdata (first file)</th>
<th>Sudbø8 (last file)</th>
</tr>
</thead>
<tbody>
<tr>
<td>patntid</td>
<td>age</td>
</tr>
<tr>
<td>131</td>
<td>75</td>
</tr>
<tr>
<td>132</td>
<td>76</td>
</tr>
<tr>
<td>133</td>
<td>65</td>
</tr>
<tr>
<td>137</td>
<td>69</td>
</tr>
<tr>
<td>139</td>
<td>78</td>
</tr>
<tr>
<td>142</td>
<td>63</td>
</tr>
<tr>
<td>144</td>
<td>64</td>
</tr>
<tr>
<td>146</td>
<td>74</td>
</tr>
<tr>
<td>149</td>
<td>65</td>
</tr>
</tbody>
</table>

Conspicuously many dates have been changed from the first to the last file. Even more conspicuous is that the year for the leukoplakia diagnosis has been changed, whereas the age for the leukoplakia diagnosis is unchanged.

Accordingly, the Commission finds that the lists to which the Commission has had access and which form the basis for the PhD project, are not correct. Neither dates, number of patients, nor other checkable observations agree to any reasonable degree with the published data and results. The Commission has tried different approaches and has made a series of other comparisons of lists, sample numbers and patient identities, etc., but the conclusion has always been the same. Neither dates for the leukoplakia diagnosis nor
the date for cancer agree with the corresponding dates in the Cancer Registry, and it is difficult to find any other explanation than that dates and lists to a large extent have been fabricated. This finding is in harmony with the Cancer Registry’s independent internal investigation. This finding is also in harmony with the Commission’s pointing out of flaws in the patient basis.

The ploidy analysis

After having decided which patients should be included in the study (allegedly 150) and which had to be excluded (allegedly 113) via the dysplasia classification, the next step was to carry out the experiment itself. This consisted of classifying the samples/blocks/monolayers from patients included in the study, to see which degree of dysplasia (mild/moderate/severe) and which type of lesion the patient had by the help of a genetic analysis – a so-called ploidy analysis; graded according to diploid/tetraploid/aneuploid. The point was to determine whether a relatively simple DNA analysis of the white patches could predict the likelihood of subsequent development of cancer.

At this time a ploidy classification was made at the Radiumhospitalet, i.e. a measurement of the amount of DNA (hereditary material) by an image-analytic machine. The analysis machine then makes a DNA histogram which draws up a person classification. The classification is subjective, even if the purpose of the machine analysis is to make it as reliable as possible and by that objective.

New England Journal of Medicine 2001 states on page 1272 that “all specimens were coded, and DNA histograms were classified in a blinded manner by four observers.” In J Pathol 2001 there are three. This is in spite of the routine at the hospital being that the classification was to be made blindly by only two independent persons.

To the Commission it has been somewhat unclear who these four independent persons were. Jon Sudbø explains that it was Wanja Kildal, Håvard Danielsen, Jon Sudbø himself, and partly Albrecht Reith. Bjørn Risberg did not take part in this classification, although he was obviously qualified for it. Risberg himself has been somewhat surprised that he was not included in this classification. Reith explains that he understood that Wanja Kildal and Håvard Danielsen made the classification. Reith further states that he himself some time later made an analysis of the histograms to see if he “was in line with WK and HED’s analyses”, but obviously he does not see himself as one of four observers, in that he refers to the fact the dissertation does not state anything about “four” observers.

It must be assumed that Wanja Kildal, who had been trained by Håvard Danielsen, was qualified to classify the samples, in the same way as Håvard Danielsen. Wanja Kildal states that she classified all the samples she received from Jon Sudbø. After Wanja Kildal had classified the samples, she showed Håvard Danielsen the first 30 classifications, in order that he could check if she had done it correctly. This
was done by Danielsen. Sudbø firmly believes that Danielsen also classified the remainder of the samples. He also alleges that a consensus meeting took place between Danielsen, Kildal and himself. Danielsen on his part is certain that he did not classify the other 120 samples, and that no consensus meeting ever took place. Based on Reith’s own statement, the Commission finds that Reith can hardly be considered as one of the four alleged observers. Whether and to which extent Jon Sudbø classified the material, seems rather unclear to the Commission. If Sudbø did classify, it is doubtful whether the classification was blinded inasmuch as Jon Sudbø and Albrecht Reith probably had access to and knew the patients’ identity and diagnosis. Principally, Sudbø denies this about the non-existing blinding. Alternatively, he alleges that since both he himself and Reith “had had access to and good knowledge of the contents of the background file from the Cancer Registry … the non-existing blinding should in such case apply also for him [Reith].” However, Reith denies that he had such access to the data material, and has accounted for this in a way the Commission finds credible. On this point, the Commission will comment that in most observation studies a “blinded” classification may be and is performed even if those who carry out the classification could have cheated by opening the blinding. In normal circumstances, one has sufficient trust in the researchers who carry out the study.

Accordingly, the Commission finds that the ploidy analysis hardly took place as described in New England Journal of Medicine 2001. On the other hand, this is not an item of crucial importance to the validity of the results, since the Commission is convinced that the samples which were analyzed comprised several duplicates, and that several blocks originated from patients who should have been excluded from the study. The ploidy analysis itself then appears to the Commission as pseudo valid, since the results were not linked with the correct number of patients that could be included.

The research result

The results of the ploidy analysis compared with cancer development, i.e. the research result itself, was astounding. The question was to which extent the ploidy in cells from white patches could be used as a sign (a predicative indicator) of future oral cancer, which is a very serious form of cancer.

Sudbø et al could show that patients with aneuploid lesions had a particularly poor prognosis, by approximately 90% developing oral cancer during a five years’ follow-up. At the same time patients with diploid lesions had a very good prognosis, by only 5% subsequently developing cancer. For patients with tetraploid lesions the probability of transition to cancer was a little above 50%. Thereby Sudbø had confirmed his hypothesis and arrived at a very good method to predict oral cancer for persons with white patches.
Based on the above, this sensational research result can no longer have credibility.

4.2.8 Other errors and flaws

In the following, the Commission will summarily point at certain other errors and defects which together and alone entail that the credibility of the three stated articles and PhD dissertation is considerably reduced.

Defective blinding

A weakness in this study is that the researcher in charge (i.e. Jon Sudbø) had full access to all patient data. This is a weakness because the study according to the articles and dissertation was to be a blinded historic prospective study, i.e. a study in which by going back in time one may follow patients’ future development. Blinded means that those who made the ploidy analyses and dysplasia classification were not to know whether the patient subsequently got cancer or not. In this case whether patients who had first got the diagnosis white patches in the oral cavity (dysplasia) at a later point in time developed cancer. Such a transformation and its frequency would be able to say something about the extent to which the ploidy in cells from white patches could be used as a sign (a predicative indicator) of future oral cancer. But because the study was an historic prospective one, one in fact had the answer on one’s hands, by knowing how many patients developed cancer. Therefore, the person who was in charge of the research itself, Jon Sudbø, should not have had access to the patient information before the classification of dysplasia and ploidy had been completed, what both he and Reith according to Sudbø himself had.

As previously mentioned, the Commission will at this point state that in most observation studies a “blinded” classification can be and is performed, even if those who perform the classification could have cheated by opening the blinding. Under normal circumstances, one has sufficient trust in the researchers who carry out the study so that the requirements as to blinding are not as stringent as in randomized studies, for example.

However, the Commission will point out that a lack of blinding as regards Sudbø, may contribute to explaining how he was able to manipulate for example the ploidy analysis in order to show positive research results, for example by including patients who had had oral cancer (and who for that reason should have been excluded). It should be noted here that another, alternative, explanation is that the analysis results have been manipulated later on.

Misleading reporting

New England Journal of Medicine 2001 page 1271 reads:
“all 150 patients had been … enrolled in a follow up-program, which, through an updated national register, had hospital-based access to the place of residency of Norwegian citizens. No upper limit was set for the duration of follow-up. Patients who were given a diagnosis of dysplasia were scheduled to have an annual examination, which included inspection of the oropharyngeal mucosa and palpation of cervical lymph nodes. Biopsies were performed at these follow-up visits if previously unrecognized white patches were detected, white patches recurred after excision, or previously recognized patches had increased in size. No patients were lost during follow-up, although data on seven patients who died of unrelated causes were censored at the time of death.”

There was no fixed follow-up program for persons with a diagnosis of dysplasia and who did not have cancer at this time. Admittedly, some patients were probably summoned to a check, but this was not done systematically, and it was not necessarily a question of an annual follow-up within the framework of a “program” either, as is the clear impression the article gives. It is also a fact that such a follow-up did not comprise all patients. However, Sudbø maintains that the program did not form part of his scientific project, but that at this time the routine at both Haukeland and Clinic for Oral Surgery and Oral Medicine was to set up a follow-up agreement a year later if a biopsy had been performed. Since this routine was institutionalized, Sudbø believes it is justified to call it a “program”.

However, the Commission finds this argumentation doubtful. The Commission furthermore is very much in doubt that no patients dropped out of the follow-up program.

The Cancer Registry has also difficulties in understanding that which is described in the article, and clearly expresses that this cannot be correct, as this is not the way things function in reality. On the other hand, obviously no others, for example coauthors, reacted to this description.

On this basis, the Commission finds that the way this has been described in the article in the best case is misleading.

Errors as regards smoking and alcohol habits

Table 1 and the text in New England Journal of Medicine 2001 refer to smoking and alcohol habits and a follow-up program for dysplasia patients. New England Journal of Medicine 2001 states on page 1272:

“Patients with confirmed use of tobacco or alcohol were given standard oral and written information on risk factors for oral cancer, and this information was repeated at each follow-up visit. Data on tobacco use were reconstructed from the medical records or by the use of telephone interviews, in which the patients were
asked about their use of tobacco at the time of the initial diagnosis of oral leukoplakia (no history of tobacco use, former use of tobacco, or use of tobacco at the time of the initial diagnosis."

The Commission has discussed this information with specialists with knowledge of this. It should be noted here that the Cancer Registry has had access to and has reviewed all the referring letters.

The material from Gade comes from hospitals all over Western Norway, from Møre og Romsdal in the North to Rogaland in the South. There is no information that the clinics who sent biopsies to Gade’s Institute participated in any form of scientific study which concerned smoking and alcohol habits or the like. Detailed information on smoking habits is therefore seldom stated on the pathologists’ referring letters, a fact confirmed by the Cancer Registry’s review.

As did these experts, the Commission believes that the information that all patients who smoked or used alcohol were advised, either orally or in writing, of the hazards they exposed themselves to, is erroneous. It may happen that clinicians – to a larger or smaller degree – informed their patients of such facts. Sudbø or other persons involved in the research project have clearly enough not been providing such type of advice, and it is impossible that they can have had access to this information, and they also never had any personal contact with the patients.

In New England of Medicine 2001 it is alleged on page 1274 that the information about smoking habits was achieved from the journals of 100 patients. A further 37 patients were telephoned and gave such information to Sudbø et al. There is nothing to indicate that such information can have been retrieved from the patient journals as alleged. There are no grounds to believe that Jon Sudbo, for example, has had access to the medical journals of these patients. Copies of the journal would in such a case have had to be sent to Sudbø, or he may have traveled across Western Norway and retrieved information that way. In any case, medical journals will often lack systematic information on smoking (not a smoker, present smoker, previous smoker). Correspondingly, there is little reason to believe that the information on alcohol use has been accessible in any systematic way.

Sudbø states that he himself, together with Puntervold and Reith, called around to the 37 patients for whom smoking data allegedly were missing, to supplement the data basis. However, no log for the carrying out of such telephone interviews exists. Sudbø has explained that information obtained in such telephone conversations was noted down on loose bits of paper and/or plotted directly into the data file. Puntervold and Reith, however, state that they have not called any patients about this. Moreover, the Commission finds it improbable that one called to a sufficient number of patients about whom there must have been a need for supplementary information. It should also be noted that 48 persons were dead in 1995, that is before the time
information allegedly was retrieved (see table in Annex 4). In other words, the Commission does not trust Sudbø’s explanation on this point.

In this context, it must be remarked that Sudbø as the main supervisor contributed with data on smoking to one of his research fellows in 2004/2005. However, the fellow has this year, right after the submission of the PhD assertion, based on this case reevaluated the data. The fellow found that there is no conformity between the data on smoking the fellow received, and the data on smoking stated in New England Journal of Medicine 2001, although the raw material is the same. The fellow found, i.a., that all the patients in the material received from Sudbø are smoking, whereas in New England Journal of Medicine 2001 there are patients (27/150) who have not had any consumption of tobacco. The fellow’s dissertation has for this reason, among others, been retained, and will probably be retracted.

The data used in New England Journal of Medicine table 1 is incompatible with data one may reasonably expect that there was access to at that time. The Commission is in strong doubt that Sudbø has had access to complete sets of data about smoking habits like he has given the impression of in i.a. New England Journal of Medicine 2001 and to his research fellow. The information on smoking and alcohol habits appears to the Commission to be partly fabricated.

In this context, the Commission finds reason to note that, in spite of flawed data, New England Journal of Medicine 2001 page 1277 states that the information on smoking was taken into account in the multivariate analysis, but that it did not influence the results. At the same time, it is stated that reliable data for alcohol use were not available for more than half the patients, and that the use of alcohol was therefore not included in the analysis. Both these points have been accounted for in an elegant and convincing manner, and reinforce the reader’s belief in this researcher, partly because the researcher appears as honest and thorough, and partly because he points out possible weak parts of his own study. This elegance in the presentation of research results may be a possible explanation of why no one found any particular reason to question and critically check the publications, more than what was done at some times.

**Double publication?**

The Commission has put the question of whether the two articles in New England Journal of Medicine 2001 and J Pathol 2001 have so many similar features that they must be considered as a double publication of the same research results in contravention of good research practice. The main results in New England Journal of Medicine 2001 and J Pathol 2001 are coinciding, but nevertheless such that the J Pathol article provides more details as regards the four pathologists’ dysplasia classification.
The Commission has submitted the question of a double publication to Reith and Sudbø. Reith acknowledges that it is a defect that there is no cross reference. However, he refers to the article in J Pathol 2001 to a much larger degree than New England Journal of Medicine 2001 discussing in-depth methodological and conceptual matters, of particular interest to pathologists. Thus Reith believes that the article has its own value and that it was not possible to include these matters in the article which was to be published in New England Journal of Medicine. Sudbø refers to the subject double publication being a relevant problem at the time of publication, which was discussed, but they concluded that it was within what was acceptable. Reith has also referred to the lack of cross reference having its explanation in both manuscripts being submitted simultaneously, and that New England Journal of Medicine does not allow cross references to articles which are submitted only. A cross reference was according to Reith regrettably forgotten at the later time when the manuscripts following several rounds finally were accepted and ready for publication.

The Commission is in doubt regarding this point, but has concluded that there was no obvious double publication. The Commission nevertheless chose to comment on this point to show that the question has been considered.

Confusion or manipulation of pictures?

Media has paid lots of attention to the fact that the same picture in New England Journal of Medicine 2001 appears twice, but is stated to represent two different patients. This is the basis for the expression of concern that the editors of the journal have published. It is a fact that it is the same picture, but in different sizes. This is an obvious error. Jon Sudbø has admitted this, but alleges that it was due to an excusable confusion.

The Commission has not considered this to be an important point and for that reason not pursued the matter further.

4.2.9 Summary

To make a thorough and checkable investigation of the actual facts has been a very difficult task to perform. This is partly because the research is advanced and based on a large amount of data which can only be understood with knowledge of technicalities linked to specialized patient studies.

Another reason that this type of investigation is very difficult is the lack of precise documentation of all steps in the research process. This problem is important and not unusual, and not unique to this case. Furthermore, sets of data and lists will exist in several versions with different names and it may be difficult to know which changes have been done, by whom and when. The investigation is further made difficult by the fact that for reasons of personal data protection and secrecy one cannot use person-unique identification of the
information, but must make use of sample numbers, preparation numbers or block numbers, and many data files are entirely without identification. In this section, the Commission will try to summarize section 4.2.7.

As stated, the Commission has concentrated its investigation on the article in New England Journal of Medicine 2001, because it is definitely the most important publication in Jon Sudbo’s research career. It forms the basis for several contemporary and subsequent original articles, i.a. a similar article published in the same journal in 2004 (New England Journal of Medicine 2004).

The main analysis and the main findings both in the 2001 and 2004 articles in New England Journal of Medicine are based on the same patient material consisting of 150 patients. Samples from these 150 patients have i.a. been classified according to DNA ploidy in samples from dysplasias in the oral cavity. This ploidy classification was in the 2001 article shown to be a strong predictor of future cancer development. This finding was reinforced in the 2004 article with a further follow-up and 11 new cancer cases.

The Commission has received the data file (Sudbo8) from MD Anderson, with confirmation that it forms the basis for the New England Journal of Medicine 2004 article by reproducing Figure 3B among other things.

This file agrees with a list the Commission has received from Reith. This list again agrees with a list (L29) which the Commission has received from Head of section Danielsen and which is produced in 1998.

Having made a thorough evaluation based on the Commission’s own review of a large number of lists and data files (Annex 3: Files_lists.doc), and the Cancer Registry’s extensive retrieval of all referring letters with relevant dysplasia diagnoses, and the reconstruction of Sudbo’s data material with the linkage that the Cancer Registry made in 1996 with a file of 226 persons (63 of 226 patients who came from Oslo were not connected at the time because they lacked personal identification numbers) as the starting point, the Commission has found the following fundamental problems with the central patient material of 150 patients used in i.a. New England Journal of Medicine 2001 and 2004 articles, and in a series of other articles:

The same patient appears several times

The 150 patients do not exist, in the sense that as far as the Commission can see, it is a matter of a maximum of 141 patients. The reason for this is that some patients are represented by several samples which in the aggregate give the number 150. Letting a patient reappear with several dysplasia samples is contrary to the description in the articles, and does not give any scientific meaning in this context. These replicas of persons are therefore invalid, and should have been excluded from the file. The Commission has not been able to determine the precise number of replicas (this is because 8 of the 150 lack block numbers on the Reith list),
but has concluded that the number of different persons in the file is at the most 141.

**Failing exclusion due to simultaneous or previous cancer**

Among the patients who the Commission has been able to identify in the Sudbø8 file there is a large number of patients who should have been excluded because they had had oral cancer prior to or simultaneously with the dysplasia in question. The Commission has found that at least 69 persons cannot be included, as they already had oral cancer at the time of the referring letter.

**Ploidy analyses have not been made for all patients**

The Commission has only been able to retrieve ploidy analyses for 69 of the observations (65 different persons) in the Sudbø8 file. This is based on lists of ploidy analyses which Puntervold has obtained from the Sudbø material (Gade/the Odontology). A far greater number of ploidy analyses (>150) have been performed, but the same patients appear several times.

**Age distribution is not correct**

The age distribution in the original material from Gade and the Odontology does not correspond to the age distribution in the material which formed the basis for the New England Journal of Medicine 2004.

Out of these four fundamental problems, it is number 2 which appears as the most serious, and which the Commission with a high degree of certainty can determine, because it is underpinned by independent information from several sources. When more than half of the central patient material is excluded, also all the results in both of the New England Journal of Medicine articles fall to pieces as well as all further research based on these.

### 4.2.10 Main conclusion

The Commission finds that Jon Sudbø has not had access to the number of patients which he states to have had, including that the dysplasia classification and inclusion process have not been made in an honest way such as described. The Commission in particular refers to the fact that out of the 150 of allegedly 263 patients included in the study, more than half of the included patients should have been excluded due to a preceding or simultaneous diagnosis of oral cancer.

It is thus evident that both articles in New England Journal of Medicine and all further research based on the same material cannot be correct or be based on reality, apart from being based on qualified guesswork. Publications based on this raw material must for that reason be retracted, see furthermore section 4.4.
There can be two explanations for the errors discovered:

- An unfortunate combination of excusable errors and misunderstandings, as well as failing competence, alertness and thoroughness.
- Scientific dishonesty, i.e. the fabrication and manipulation of research data and consciously misleading research reporting.

The Commission finds that the errors and defects discovered are too many, too large and too obvious to be ascribed to excusable errors, incompetence or the like. The Commission finds that data have been manipulated and fabricated, and probably adapted to the findings one wanted to arrive at.

The Commission finds that Jon Sudbø has been alone in the manipulation and fabrication of data. The Commission will revert to this in more detail, however, including other players’ role in the continuation, see in particular Chapter 5.

*Based on the account given above, the Commission finds that there is scientific dishonesty on the part of Jon Sudbø related to the PhD dissertation, New England Journal of Medicine 2001, Oncology 2001 and *J Pathol* 2001.*

### 4.3 After the presentation of the thesis

After having defended his thesis at the University of Oslo on March 9, 2001, Jon Sudbø continued his scientific activity, within the same field, i.e. oral cancer. This resulted in a series of scientific original articles, reviews, readers’ letters and the like, which were published currently in several renowned medical journals.

In connection with the publication of the research results in *New England Journal of Medicine* 2001, Reith and Sudbø in a letter to the Norwegian Board of Health wrote that the research results should lead to a changed practice as regards screening and treatment of patients with white patches in their oral cavities in Norway. By this, many patients could be saved, was the allegation. They also mentioned the need for a prospective study. The Board of Health replied that they did not have any opportunity to reorganize treatment practice in Norway, due to a lack of resources, among other things. The Board of Health also referred to the fact that support for a prospective study would had to be applied for to other quarters.37

Concurrently with the publication of *New England Journal of Medicine* 2001, *Dagens Medisin [an independent newspaper for the health sector]* on April 26, 2001 reported a “Breakthrough in the battle

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against oral cancer”. “Between eighty and ninety percent of all cancer developments can be predicted by chromosome analysis” Sudbø is supposed to have stated to the newspaper.

In an editorial written by Scott M. Lippmann and Waun Ki Hong (with whom Sudbø subsequently initiated a collaboration) in New England Journal of Medicine 2001 in the same edition of the journal, the study was called an important progress as regards the assessment of the risk of oral cancer for patients with leukoplakia. The editorial states:

“The new molecular data have important implications for the standard of care of patients with oral leukoplakia. Local management ranges from watchful waiting to resection with widely varying margin widths, depending on histologic and clinical features. Molecular information can redefine the assessment of the risk of oral cancer and even guide treatment, with the one important caveat that the molecular results involving patients with severe dysplasia in the studies we have discussed may have been confounded by the small numbers of such patients and the likelihood that they underwent more rigorous surgical procedures than did the patients with mild or moderate dysplasia. It is time to establish standard molecular assays to help plan the management of oral leukoplakia. … Confirmation of the completeness of resection, close monitoring, and chemoprevention trials would be appropriate approaches for patients deemed at high risk on the basis of molecular assays, including patients with hyperplasia.”

In 2001, Jon Sudbø applied to the Cancer Society for money for the project ”Early diagnosis and treatment (chemo prevention) of early stages of oral cancer” for 3 years. The application was denied.

At the same time he also applied to Health and Rehabilitation [a foundation granting money to voluntary organizations and efforts to improve physical and mental health in Norway] via the Cancer Society for funds to the project “Protocol – prevention of oral cancer”. He obtained funds for this project for the years 2002-2004. He was later on also granted funds for 2005.

In 2001-2002, Jon Sudbø also came in contact with American researchers within the same specialist field. Reith and Sudbø met with Scott Lippmann from MD Anderson personally for the first time in November 2002 during a conference in Frankfurt. According to Reith, it was Lippmann who suggested the collaboration which was initiated. This collaboration led to several publications in leading medical journals, as for example New England Journal of Medicine in 2004 and The Lancet in 2005, see section 5.3.

Thus, in 2001 Jon Sudbø had started the work with what was to become part of a big project application to the National Cancer Institute (NCI) in the USA. The project was granted 10 million dollars, of which most went to MD Anderson in the USA.

The Commission will revert in more detail to this PROTOCOL study in section 5.3, but will first account for the consequence of the main conclusion in 4.2.10 for other publications.

4.4 Other publications

In the following, the Commission will deal with the articles suffering from such substantial defects and doubts that they cannot be considered valid, and for that reason should be retracted. The Commission has reviewed the 38 publications which resulted from an individual search for Jon Sudbø in January 2006 in the PubMed data base, see Annex 1. The Commission realizes that this publication list is not exhaustive, but has nevertheless found reason to base itself on the list as it in all probability comprises the most important works. Sudbø has not commented on the draft for this section in particular, but refers to the comments cited above.

The Commission refers to the main conclusion in section 4.2.10 and to the general account of retraction of scientific publications in section 3.6.

In the following, the Commission will deal with the publications in which the Commission has found errors and the like. Of most interest are Sudbø’s original articles, totaling 12. By an original article is meant that the article comprises original research results which are not presented previously. It is such articles that are the most important and most meritorious within the research communities. When reviewing the PhD dissertation which contains 6 original articles, the Commission previously found that three original articles must be retracted, whereas no errors were found in three original articles, cf section 4.2. In this section will be held that a further 5 original articles must be retracted or at least be subject to an expression of concern for their validity. This means that 8 out of 12 works appear as more or less invalid. Out of Sudbø’s original articles there are only the three first articles in the PhD dissertation that are found not to contain errors, see section 4.2.5, as well as a less sensational article published in Oral Disease 2003. Accordingly, there is a basis for stating that the essential parts of Jon Sudbø’s scientific production suffers from errors and flaws caused by scientific dishonesty.

The publications which are not found to contain errors, apart from four original articles, mainly concern lesser reviews and letters of less scientific value, as well as works in which Jon Sudbø has only been a coauthor, i.e. publications which mainly have been prepared by others.

- Sudbø J, Warloe T, Aamdal S, Reith A, Bryne M. Diagnostikk og behandling av forstadier til munnhulekreft [Diagnosis and treatment of oral precancerous lesions]
  Tidsskr Nor Laegeforen 2001;121:3066-71. Overview article.

39 www.pubmed.gov
The article is an overview article that summarizes results from Sudbø’s articles included in his PhD degree. The article is therefore based on raw data which the Commission has found are manipulated and partly fabricated, cf section 4.2. The article must therefore be retracted.


  The article asserts that it is based on analyses of a material that has not been used in previous publications. The PhD dissertation states that material from 263 persons was collected and that 21 of them were excluded from the original study due to having red patches in their oral cavities (erythroplakias). It is persons with erythroplakia that have been studied in this study. In the method part it appears that the material comprises 57 samples with human biological material from 37 patients with erythroplakia collected in the period 1988-2000. The Commission here refers to the fact that it has not found any indications that these raw data exist.

  In its other findings, the Commission has found that so much doubt is linked to whether these raw data in fact exist that it is reasonable to apply a large question mark to this article.


  The article is a review of Sudbø’s own research results. That means that it is based on the raw material which the Commission has based itself on, cf section 4.2. The article must for this reason be retracted.


  The article is a review which is based on Jon Sudbø’s earlier research results, which again are based on raw data that are manipulated and partly fabricated, cf section 4.2. The article must for this reason be retracted.

The article is a review which is based on Jon Sudbø's earlier research results, which again are based on raw data that are manipulated and partly fabricated, cf section 4.2. The article must for this reason be retracted.


The article is a review which is based on Jon Sudbø’s earlier research results, which again are based on raw data that are manipulated and partly fabricated, cf section 4.2. The article must for this reason be retracted.


The study is based on an analysis of the raw data which form the basis for parts of the PhD work and which are manipulated and partly fabricated, cf section 4.2. The article must therefore be retracted.


The article is a review based on the raw data collected during the PhD degree work and which are manipulated and partly fabricated, cf section 4.2. The article must therefore be retracted.

The article is based partly on the raw data collected in connection with the PhD degree work and which the Commission has found are manipulated and partly fabricated, cf section 4.2. See in particular under section 4.2.7 in which the Commission accounts for the comparison of the data list used in New England Journal of Medicine 2001 and New England Journal of Medicine 2004. In addition the article is based on a follow-up of the same patients which did not take place. The latter fact is partly admitted by Sudbø to the Commission. The article must therefore be retracted.


  The article is a review of earlier research and based on material used both in New England Journal of Medicine 2001 and New England Journal of Medicine 2004. The Commission has determined that this material is manipulated and partly fabricated, cf section 4.2. The article must therefore be retracted.


  The article is based on allegedly newly collected material from 275 persons. This material is supposed to have been collected via dental clinics. The Commission has tried to obtain documentation showing that these raw data in fact exist. The Commission has been in contact with, i.a., the dentists that are listed as coauthors because they had assisted in collecting material from their patients. These dentists confirm that they were asked by Jon Sudbø to collect scrapings from patients. However, they only collected 10-20 samples each. It therefore appears as rather unlikely to the Commission that Sudbø can have had a complete data material from 275 patients. The Commission also finds it quite unlikely that these patients were enlisted in a program for smoking cessation with a further follow-up. No indications have been found that such a program was implemented. The cited dentist colleagues have difficulties in understanding that such a program existed. The Commission’s
assessment must also be seen in light of other deviations from good scientific practice which the Commission has detected.

Jon Sudbø has admitted that cotinine level was not measured for all patients that participated in the study. The latter fact alone means that the study cannot any longer be considered valid. The journal has published an expression of concern relating to this article and the editors state that with the exception of Sudbø and Reith, none of the coauthors participated in the preparation of the manuscript and they therefore do not meet the authorship criteria. In the Commission’s view, the article should be retracted.


The article is a review of earlier research in which reference is made to the original raw data collected in connection with the PhD dissertation and which are manipulated and partly fabricated, cf section 4.2. The article must for this reason be retracted.


The article is based in its entirety on fabricated raw data and is for that reason already retracted. These facts have been admitted by Sudbø. The Commission has for this reason not spent much time on investigating this article. However, the Commission got access to the correspondence between Jon Sudbø and J. Jack Lee of MD Anderson. Thereby the Commission detected how these new raw data came about, see section 5.3.
5. Possible explanations

5.1 Introduction
In Chapter 4 the Commission found that the raw material which formed the basis for the main part of the PhD project, is manipulated and fabricated. This contributes to a series of later publications having to be disregarded. The Commission has also found several cases of data manipulation and fabrication in the subsequent scientific career of Jon Sudbø. The Commission found that this was due to scientific dishonesty on the part of Jon Sudbø.

The comments that Sudbø has given to the draft report did not provide the Commission with reason to make substantial changes to the preliminary conclusions reached during the investigation.

The Commission has not found grounds to believe that others have participated in manipulating and fabricating research data or in any other way committed scientific dishonesty, as this is defined in the recently adopted Research Ethics Act section 5 (2) (not yet in force).

In its terms of reference, the Commission was asked to seek an explanation of the facts discovered. The Commission has asked itself how these – in retrospect – obvious and gross acts could take place, in collaboration with a series of well qualified coauthors and collaboration partners, and at a renowned research institution.

In introduction, the Commission will emphasize the obvious, namely that there will always be a possibility for the dishonest person to cheat and defraud others. No system is water tight in this respect, and this also applies to Norwegian research. The question here is first and foremost whether it is possible to identify factors that have contributed to the acts discovered by the investigation.

The Commission has by no means any foundation for drawing definite conclusions about what caused these circumstances. However, the Commission finds reason to point out certain factors which may contribute to illuminate how and why “things turned out as they did”. To the Commission, a part of the explanation is that a series of “unfortunate” factors occurred simultaneously, and these must be seen in context to illuminate the case.

Criticizable facts are summarized in Chapter 7.

5.2 The PhD project and further research
The Commission has got the clear impression that Jon Sudbø acted relatively freely and independently, both as a research recruit (research fellow) and researcher. This impression is confirmed by several of Sudbø’s
colleagues. Reith explains this by Jon Sudbø appearing as an exceptionally clever PhD candidate and that he was also relatively experienced and not as young as many of the other research fellows. In his comments to the draft report, Sudbø objected to Reith’s description of Sudbø’s relatively free role, and in that connection pointed out that he had little or no experience as a researcher at the time when he started his PhD project. Sudbø conceives this as an attempt by Reith to disclaim responsibility.

The Commission’s total impression based on the information that has come to light during the investigation, is all the same that Reith seems to have had an active but nevertheless relatively superficial role as a supervisor. Reith seems to have observed what went on and discussed this underway with Sudbø, without having been involved in the analyses and treatment of data as such. Nor can he have carried out random checks or suchlike to ensure quality. It seems as if Reith has replied to questions from Sudbø, but not himself put control questions or the like. However, Reith has provided contact with both the Cancer Registry and Gade and thus been a key initiator and door opener. Then he has allowed Sudbø to work independently with the data analyses themselves. The Commission here refers to the fact that Sudbø as mentioned got access to both the material and the patient data. This made it possible to manipulate and change around data lists, blocks and analysis results without anyone discovering it. In light of the description of the facts in Chapter 4, the Commission finds reason to state that Reith should have been more alert as a supervisor and followed Sudbo’s treatment of the data material more closely and not least checked to a larger extent certain factors that are erroneously described in publications in which he is listed as a senior author.

Another element which may provide a certain explanation of the facts that have been discovered during the investigation, is that no formal approval or review of the project exists at all. No permissions, evaluations from the Norwegian Board of Health (now: The Directorate for Health and Social Affairs), the Data Inspectorate/the Norwegian Social Science Services or the Regional Committee for Medical Research Ethics exist, something which also contributes to elude further investigations and quality assurance of the project. As mentioned above, this flaw is something for which Sudbø himself, Reith and the Radium hospitalet must assume the responsibility.

However, the Commission will underline that there is no reason to believe that such failing compliance with the formalities has been a conscious strategy in order to be able to carry on a dishonest research activity. The explanation of these circumstances seems mainly to be that sufficiently effective and good enough routines have not been in place as regards the control and supervision of research projects at the Radium hospitalet. The fact that Sudbø did not have a formal employment relationship to the Radium hospitalet, is evidently enough no acceptable explanation. The Commission has indeed found (section 4.2.3) that the research took place under the auspices of the Radium hospitalet and that this institution had the overall responsibility for Sudbø’s research activities. Even if instructions and control bodies existed at the
institution, it does not seem as if these were satisfactorily implemented. The project was not submitted to the Protocol Committee, for example, and no one saw reason to question it. Researchers associated with the department indeed seem to have had a relatively relaxed relationship to the formalities. This applies in relation to the retrieval, delivery and treatment of human biological material and sensitive patient information, recommendations from the Regional Committee for Medical Research Ethics, licenses for data processing and dispensation from the duty of secrecy. The Commission has also found reason to express doubt as to whether the organization of this research project has been defensible. This organization is an institutional responsibility.

Furthermore, it may seem that when someone was worried that quality routines may not have been followed, this was not followed up by the management or colleagues, maybe because one did not have any system or tradition regarding this type of warning. It must be noted here that one person retained all the documentation from the contact with Sudbø, exactly because this person had his/her suspicions. This was at the end of the 1990’s. However, the person concerned did not want to get into a difficult “whistleblower position” and therefore refrained from making further investigations.

Concerning the relationship to coauthors, what happened in connection with the publication of New England Journal of Medicine 2001 is apparently characteristic of Sudbø’s choice of and collaboration with coauthors in subsequent works. The Commission here relies on written and oral feedback from almost 60 coauthors. A possible explanation of why the research cheating was not discovered earlier may partly be found in the fact that the coauthors mainly appeared as sub-suppliers or as senior guarantors (i.e. senior researchers who primarily played a central role on the overall level (idea, planning, compilation and the like) and who by reason of their professional weight have contributed to giving the works a professional legitimacy). Moreover, the authors have mainly related to Sudbø. In other words, there has apparently not been much communication “horizontally” between the various coauthors or research groups. Most of the communication took place via Sudbø. Sudbø has pointed out that he did not prevent communication between the coauthors in any way, but the Commission cannot see that he has contributed to or has called for such a contact between the coauthors. In this way, Sudbø has been in control of which set of data, which information and the like the individual coauthor possessed. It is worth pointing out that this information probably was limited. None of the coauthors seem to have had access to the underlying data material and patient data. They have probably not seen this as a natural or obvious part of the assignment given them either. However, such a distribution of work is not an unusual phenomenon in medical publications – a fact that obviously must be taken into account in the assessment of whether there is a basis for criticizing the coauthors. As an
example of this, reference is made to the collaboration between Jon Sudbø and J. Jack Lee in connection with the article which was published in New England Journal of Medicine 2004:

At one time Sudbø sends a radically changed file to J. Jack lee at MD Anderson\textsuperscript{41}. The file shows “data cleaning along the way” as expressed by Lee in an email to Gunnar Sæter of January 13, 2006 after this case had become known. The Commission has compared two files: a) “sudbo8” which is the file that was used in the article in New England Journal of Medicine 2004 and b) “updated rawdata” which according to Lee is the first file he received from Sudbø for the 2004 article. The comparison was based on the variable patnid (patient number) which is on both files. The Commission has included the following variables: age, tobacco, year leukoplakia and year cancer. An excerpt of the 150 observations is provided in Table 3 in the report. As previously mentioned, it is conspicuous that “year leukoplakia” has changed from the first to the last file without age having changed. This is mathematics which does not tally if age is age at leukoplakia. In an email from Sudbø to Lee of August 8, 2003 Sudbø writes: “One point: the age of the subjects have been recalculated to what they were at the time of initial diagnosis”. The latter ought to mean that age at leukoplakia is what is concerned, see section 4.2.7.

On a general basis, the Commission finds reason to note that many research fellows and researchers will have the opportunity to manipulate and even fabricate raw material, without either supervisors or coauthors being able to discover it. Research is indeed to a large degree based on trust, as it necessarily has to be. It is important and necessary that researchers have trust in one another, that one may trust that what others supply is genuine. The employer must be able to trust its employees, and journals must be able to trust researchers. Research participants and the public in general must also have trust in researchers. But such trust cannot be without limits. There must be a certain control and sound skepticism, because at one time or another warning lamps should start to flash thereby causing checks and controls to be made. But the fact that very few researchers find it obvious that any of their partners will fabricate research data may explain something of that which in retrospect easily may appear as failing alertness.

On the other hand, there are, as the Commission sees it, certain descriptions in the articles which more people should have reacted to. This may be coauthors, supervisors, superiors, critics, colleagues and others. The Commission would in particular refer to the account of the reclassification of the dysplasias which allegedly was made by four independent pathologists,\textsuperscript{42} as well as ploidy analyses which allegedly also was made by four independent observers.\textsuperscript{43} This was neither usual nor the case. The Commission also refers to the allegations relating to the reporting to the Cancer Registry, a follow-up program for patients and the allegation that one was in possession of almost complete smoking data. These are matters which one maybe

\textsuperscript{41} Dataliste: "updated_rawdata_renamed_sudbo8.xls"
\textsuperscript{42} “All histologic sections were subsequently reevaluated by four pathologists according to the guidelines of the World Health Organization”; NEJM 2001 page 1272.
\textsuperscript{43} “All specimens were coded, and DNA histograms were classified in a blinded manner by four observers”; New England Journal of Medicine 2001
In retrospect should be able to say that someone should have discovered, or at least put a question mark at – both inside and outside the professional community at the institution, taking into account that this information was published in the internationally most renowned medical journal, namely the New England Journal of Medicine, which is remarkable for Norwegian researchers. At the same time, it must be admitted in the coauthors’ defense that the supervisor as well as coauthors in conversations with the Commission has had difficulties in and used much time to reconcile themselves with articles, which they themselves had taken part in and felt ownership to, being in fact based on fabricated data. The latter shows how unbelievable and unusual fabrication of research data in Norwegian research communities is perceived to be by researchers.

5.3 In particular about the NCI application and Lancet article

During the period 2000-2001 Jon Sudbø and Albrecht Reith as mentioned got the idea for a new and larger study. Also this study was related to the prevention of oral cancer, but this time it was to be a prospective study in which they were to follow patients forward in time. The study was named PROTOCOL, which stands for *Prospective randomized trial on preventing oral carcinomas from oral leukoplakia*.

In 2000/2001 Jon Sudbø prepared a protocol. Following internal discussions at the Radiumhospitalet it was suggested that the protocol should be translated into English, as the potential was considered to be big, and that it ought to be an international study. Jon Sudbø translated the protocol himself in the summer 2001.

At the same time Sudbø and Reith applied for support to the project from Health and Rehabilitation via the Cancer Society. They were granted funds for the years 2002 until December 31, 2005.

In 2002-2003, Jon Sudbø and Albrecht Reith were fairly often in the USA for seminars and the like. In that connection they came into contact with Scott Lippmann and the professional community relating to MD Anderson, as well as Andrew Dannenberg of Weill Medical College at Cornell University. This contact gradually developed into a professional collaboration. This collaboration resulted in agreement to apply to National Cancer Institute (NCI) for funds for a large study. Sudbø’s PROTOCOL study was to be included as an element in this study. The application was submitted to NCI in the summer of 2003.

Jon Sudbø has stated that at the same time, that is in the beginning of 2003, he started working on the data list which later on was to form the basis for the article in The Lancet, which has a certain connection to the NCI study by a preliminary version of these data being included in the application according to Lippmann, but without having a central role. Jon Sudbø has stated to the Commission that the basis for this data list is a series of data published under the auspices of the Cancer Registry and the Norwegian Institute of Public Health, among other institutions. These are data relating to tobacco habits, cancer and other relevant factors.
Thus, he made a table of cancer incidents in various age groups and various periods of time, and then entered tentative dates of birth for fictitious patients. In other words, the list is based on qualified guesswork. The list was supplemented by fictitious use of NSAID, various types, various doses, various time intervals, such that one could see how various factors were distributed on patients and the control group, with different risk of getting oral cancer based on smoking habits. Sudbø has stated that this originally was meant as a pure simulation data base – i.e. fictitious number experiments. Nothing has come to light to indicate that other persons knew about this.

The further time and sequence of events are somewhat unclear to the Commission. However, the Commission has had access to the comprehensive correspondence that took place between Jon Sudbø and the bio statistician at the MD Anderson, J. Jack Lee. This correspondence documents in detail how Jon Sudbø managed to produce the fabricated data file which forms the basis for the Lancet article. The communication between Sudbø and Lee per email with data files attached, shows how Jon Sudbø first sent a fictitious data file to J. Jack Lee.

The Commission will not discuss this in detail, but would emphasize that the common theme in the correspondence is that J. Jack Lee points out errors, defects and inconsistent factors in the file he had received. Then Jon Sudbø accounts for how he will have these regrettable errors corrected, errors which according to Sudbø must be based on misunderstandings and other unfortunate circumstances. According to Sudbø’s accounts per email to Lee, the correction of errors was made in cooperation with qualified specialists and institutions. An email of January 29, 2005 states, for example:

“I checked also with the health survey people, who scrambled on Saturday. The confirmed alcohol was not a selection criterion for the original search.”

Jon Sudbø writes in an e-mail of March 29, 2005 to Jack Lee:

“Albrecht and I will be in meetings with CONOR (Cohort of Norway), the consortium which administers the databases of the health surveys. We need to make sure we have documented all there is to document regarding these surveys and how they are linked to other population based disease registries.”

Another example of Sudbø demonstrating his will to work day and night with this project and his access to not only competent specialists but also to the registers in Norway is in an email dated June 6, 2005, in which he writes to Scott Lippman, J. Jack Lee and Andrew Dannenberg:

“Please find attached clean copies of the NSAID paper, cover letter and responses. Jon Mork and I spent most of the weekend at the Cancer registry, checking the number of cases with cancers in different locations of the oral cavity. We have also had a meeting to go over the final drafts of the paper, responses and cover letter.”
An e-mail of September 30, 2005 states:

“Tonight, I have gone through and discussed the commentators viewpoints and the responses from Jack, with epidemiologists at the Cancer Registry. They ([N.N.], lead epidemiologist on Jon Morks 2001 NEJM paper, and [N.N.] also epidemiologist at the Cancer Registry and on the Mork 2001 paper) found the responses to the point, and well placed. In other circumstances, this should get us on dry land with respect to acceptance.”

It must be noted that the Commission is of the opinion that it is not likely that these meetings took place, or that Sudbø or any of the mentioned persons had such access to the Cancer Registry and such information.

The application to NCI was granted in March 2004, and the total grant was for approximately NOK 70 million. However, the project is mainly an American project directed by Scott Lippmann and MD Anderson. Jon Sudbø’s PROTOCOL project only got a small part of this grant. According to Sudbø, at least NOK 16.5 million was to be transferred to the Radiumhospitalet in the course of a five years’ period. He refers to the Norwegian project being one of four projects included in the total application (a so-called Program Project Grant).

In the summer and autumn of 2004, an application was made to the Regional Committee for Medical Research Ethics South Norway (REC-South) and the Data Inspectorate for approval of the PROTOCOL study. The study was approved on August 13, 2005 and October 19, 2004, respectively.

The PROTOCOL study was opened for inclusion of patients in December 2005. When it became known through media that the Lancet article probably was based on fabricated research data, this study was stopped for an indefinite period of time. No patients had then been randomized (included) in the study, but five patients had been through introductory interviews. One patient had according to Sudbø been subject to a surgical biopsy for assessment with a view to randomizing in the study.

The Commission has reviewed the NCI application and the material delivered by Jon Sudbø. The application is based on Sudbø’s raw material, which partly consists of fabricated data. There is nothing to indicate that any of the collaboration partners knew of or had any suspicion about this. Jon Sudbø also gives the impression that he can supply data and analyses, which, at least in retrospect, it is relatively obvious that he would not have been able to supply. He also states that he has received public permissions which are obviously fictitious. In this connection, the Commission refers in particular to page 130 of the application, where a series of essential points appear as pure fiction [the Commission’s running commentaries are included in square brackets]:
Accrual Infrastructure, Feasibility

Project 1 leader Dr. Sudbo and Core C Co-Leader Dr. Reith built over a 10-year period the infrastructure that will support clinical Project 1 and its translational interactions with PO1 colleagues at M.D. Anderson and Weill Medical College of Cornell University (Dr. Dannenberg).

- **1993-4:** Access to biopsy specimens from all Norwegian pathological departments approved by the Norwegian Cancer Registry (Kreftregisteret), Norwegian Data Protection Agency (Datatilsynet), Norwegian Department of Health and Social Security (Sosial- og helsedepartementet). [This appears in all essentials as pure fiction, cf section 4.2.]

- **May 1995:** Access to Norwegian Cancer-Registry data for evaluating follow-up of 150 patients with oral white patches. [The date should have been from the beginning of 1996, and the material referred to is partly manipulated and fabricated, cf section 4.2.7].

- **January 1997:** Access to this information granted by the Regional Ethical Committee (Regional Etisk Komité), Norwegian Data Protection Agency (Datatilsynet), and the Internal Advisory Board at the Norwegian Radium Hospital (NRH). [All this is incorrect, cf 4.2.4]

- **January 1998:** Permission from the Norwegian Data Protection Agency (Datatilsynet) to do telephone interviews to get additional epidemiological information regarding smoking and alcohol habits and comorbidity from persons in the study. [Incorrect, cf 4.2.4]

- **February 2003:** Epidemiological data on NSAID effects obtained from The Norwegian Cancer Registry and National Health Survey Project. [This is pure fiction.]

In this context should be noted that in the application, Jon Sudbo demonstrates that he has a full overview of the formal procedures which apply to this type of medical research projects.

While the raw data gradually took form through the cooperation with an obviously unsuspecting J. Jack Lee, Jon Sudbo started work on the article which subsequently was published in The Lancet. A draft article was first sent to New England Journal of Medicine, which rejected it twice. The Commission has not been given access to the referee opinions. The article was then finally published in The Lancet in October 2005, after having been through a so-called fast-track referee system. It is worth noting that one of the professional colleagues, who reviewed the article, was highly negative to its publication.

The main results that were subsequently published in the Lancet article are to be found in a power point presentation by Dr. Ernest Hawk of National Cancer Institute in the USA from a FDA hearing in the middle of February 2005.

On April 7, 2005, American health authorities (FDA) warned against cardiovascular side effects of non-selective NSAIDs. European health authorities were more reserved, and the Commission does not know of any changes to the guidelines having been made. According to the press, the Norwegian Medicines’

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44 www.fda.gov
Agency is giving priority to the case, but as far as the Commission knows no changes have been made to the Norwegian guidelines.

On April 7, Aftenposten [a major Norwegian daily newspaper] spent half its first page to report that Ibux (ibuprofen) could lead to heart disease. On May 3, Jon Sudbø is supposed to have stated to Adresseavisen 45 [another Norwegian daily newspaper] that he “had to triple check the data because he could not believe they were correct. But they are water tight.” Jon Sudbø is unable to understand this press coverage.

5.4 Questions are raised in relation to the ploidy classifications

In the summer 2005, Jon Sudbø was contacted by Bjørn Risberg who wanted to use the raw material on which Jon Sudbø’s PhD work was based in another study. In this connection, Risberg repeated parts of the ploidy classifications. It appeared that these in no way agreed with the classifications on which Sudbø had based his work. Risberg, together with Eva Sigstad, pointed this out to Sudbø in a letter dated August 3, 2005, at the same time as they asked to be delivered the data material used as basis. In the letter is stated:

“We have now made up the results from our automatic measurement of your previous M41 study (on oral mucosa biopsies) and compared with the results you arrived at by automatic measuring. The results are as follows:

<table>
<thead>
<tr>
<th></th>
<th>Manual</th>
<th>Automatic</th>
<th>Same ploidy result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diploid</td>
<td>29</td>
<td>36</td>
<td>18</td>
</tr>
<tr>
<td>Tetraploid</td>
<td>15</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Aneuploid</td>
<td>13</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Unsuited/no block no.</td>
<td>24</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>81</td>
<td>25</td>
</tr>
</tbody>
</table>

There is a large discrepancy between the results. The cause of this can be several:
1. wrong rendering of the data in the data bases
2. measuring errors; degenerated (“old”) material in the automatic measurement
3. differences of method between manual and automatic

It is essential to find the cause of the discrepancy. Further automatic measurements will otherwise be without value. We would appreciate hearing your views on this problem.”

The Commission will comment to this that Risberg’s and Sigdal’s measurements are in harmony with the Commission’s previous findings under section 4.2.7, in the sense that Sudbø’s measurements do not agree when they are checked. In the Commission’s opinion, Risberg’s and Sigdal’s letter is striking, by showing

45 http://www.adressa.no/nyheter/sortrondelag/article499549.ece
conformity in only 25 out of 81 measurements. It is obvious that this was a very serious and dramatic accusation against a research colleague in spite of the neutral wording of the letter. In the Commission’s conversation with Risberg it appeared that by going further into the raw material for ploidy analyses, it appeared that there was an acceptable conformity between the automatic and manual measurements (which was the original purpose of Risberg’s investigation) and that any discrepancy would have to be explained by an exchange of patient identification. According to Risberg, the latter was never clarified.

According to Risberg, Sudbø tried to explain away all of this, and said he would put things straight, but this never happened. Risberg brought this up with the department manager, Jahn Nesland, but nothing came out of it. At this time, the Radiumhospitalet was busy with a very demanding merger with the Rikshospitalet.

Jon Sudbø contests this presentation, and asserts that it was a joint evaluation by himself, Risberg and Reith which led to the reclassification. The Commission does not believe Sudbø’s explanation on this point. Also Reith has confirmed that, when Risberg wanted to reclassify the material, it proved difficult to obtain the material from Sudbø. After several reminders, Reith suggested that Risberg wrote a letter to Sudbø to make him give priority to obtaining the material. Finally, Reith did obtain agreement from Sudbø for a meeting, a meeting that Sudbø nevertheless did not attend. The letter from Risberg and Sigstad of August 3, 2005, was unknown to Reith until the case was discovered in 2006.

As regards the choice and involvement of coauthors to works produced in a later phase, where Sudbø was more established as an independent researcher, it is, like in the first phase, typical that these coauthors have had marginal knowledge of the raw material. At the same time, Sudbø surrounded himself with a sufficient number of persons for his project to appear as legitimate. It seems to the Commission as if the coauthors to a large extent were used to legitimize what Sudbø did. It is also typical that the coauthors have had little or no contact among themselves; it is Jon Sudbø who had the full control of what each of them knew, and to what each of them had access. In several cases, the coauthors did not see the final draft of articles, and many of the coauthors were very little involved in the writing of the manuscript itself.

5.5 External factors

In compliance with its terms of reference, the Commission has examined and evaluated whether external causes can have contributed to the breaches of good scientific practice that have been discovered. It may be a question of several causes, as for example the relationship to external cooperating research institutions, including the pharmaceutical industry.

The Commission has evaluated such factors, but has not found grounds for believing that external factors of this nature contributed to the breach of good scientific practice. Nor has the Commission discovered actual facts which have provided reasons to implement more extensive and in-
depth investigations on this point. For example, the Commission does not find it likely that Jon Sødbø produced research data and results commissioned by the pharmaceutical industry.

However, the Commission cannot entirely disregard as a possible cause that Jon Sødbø may have been driven by a wish to satisfy express or unspoken needs, wishes or such like from international cooperation partners, including the pharmaceutical industry, with ensuing honor and recognition, as well as financial support to new research projects. The Commission cannot exclude that interests of this nature to some extent may be an explanation (motivating factor) on the background of the NSAID findings, i.e. the cardiovascular results in the Lancet article. These were results that were sensational and potentially useful to several international main players within the development and manufacture of medicines.

Moreover, there is reason to point out that the type of dishonesty that manifests itself in, i.a., the NCI application and the Lancet article is possible precisely because one cooperated with external institutions with insufficient knowledge of the situation in Norway.

5.6 Flaws in sets of regulations and similar formal types of control

The serious breaches of good scientific practice discovered in this case, are in all essentials breaches of fundamental and unambiguous rules which have existed for a long time. The prohibition against improper manipulation and fabrication of research data is embedded in rules that all researchers must be assumed to be well acquainted with. Therefore, the Commission cannot see that the facts discovered are due to a lack of rules.

On the other hand, the Commission has discovered a series of minor breaches, which in aggregate have contributed to a system in which the breaches of good scientific practice have been allowed to increase without being discovered earlier. But also here it seems, in the Commission’s opinion, not to be the lack of rules which is the problem, but rather the individual researcher’s and institution’s knowledge and practicing of the rules which actually exist. The Commission would here as an example refer to the fact that the PhD project should have been submitted to the Regional Committee for Medical Research Ethics, the Data Inspectorate and the Norwegian Board of Health (now: The Directorate for Health and Social Affairs) and that these are factors no one has reacted to, neither coauthors, supervisor(s) or the management of the institution, nor those who were responsible for approving the PhD degree.

The Commission’s findings on this point are in harmony with three studies related to the regulation of medical research:

In its concluding report from 2001, the then National Committee for the Evaluation of Dishonesty in Health Research stated that it was important to have clear rules for good scientific practice. One therefore prepared a guide to the implementation of projects in medical and health research. The committee was concerned that such thematic should form part of the mandatory part of the research education, but believed
that it was just as important that an environment for lifelong learning within research ethics and good 
research practice should be developed. The committee underlined that the responsibility must lie with 
education institutions and research environments themselves, but that a central initiative to initiate the process 
was needed.

This is moreover in harmony with the Nylenna Committee’s report from 2005 on the regulation of 
medical and health research.\textsuperscript{46} The Nylenna Committee found that it was not primarily the lack of rules that 
was the problem, although certain deficiencies existed. The main problem was in the committee’s opinion 
that the rules were fragmented, complex and inaccessible, and that few people had an overview of the set of 
rules. Simplification and clarification of the set of rules and bureaucracy, as well as making the research 
institutions more clearly accountable, was the Nylenna Committee’s main recommendation for measures.

This approach was also given weight in the preparatory works to the Research Ethics Act.

Thus, the Commission’s opinion is that the facts discovered are not primarily related to a lack of 
rules, but rather that there has been a lack of measures to prevent breaches of good scientific practice through 
the implementation of simple and effective routines. The latter is first and foremost an institutional 
responsibility. The Commission has in fact noticed that over the last years there has been an increasing 
awareness of these factors at several research institutions, among others at the 
Rikshospitalet/Radiumhospitalet MC, which has implemented a series of measures to guide researchers.\textsuperscript{47}

relating to medical and health research that involves humans, human biological material and health data (Health 
Research Act)

\textsuperscript{47} See www.klinforsk.no. For Aker University Hospital, see www.forskningsjus.no, and for Ullevål University Hospital 
refer to http://www.ullevål.no/modules/module_123/news_template_avdeling.asp?iCategoryId=664
6. Possible consequences

6.1 Reflections on consequences for research

The fabrication of research data is counted among the most serious forms of dishonesty in research. When such things occur, it contributes to a general weakening of the society’s trust in research. For medical and health research, this doubt about trust may also have consequences for the trust in the health services in more general terms. Such doubt may create insecurity and concern in the population. The researcher community is highly dependent on society’s trust, both to ensure that there is a political will to use public budgets to fund research, and that the population will be willing to participate in various research projects.

The Nordic countries have traditionally had a positive reputation within clinical as well as epidemiological research. Based on these countries’ health and disease registers, and the possibility of linking data to comprehensive population registers with unambiguous identification opportunities, the Nordic countries traditionally have been sought after as collaboration partners in research projects. For small countries, this type of research collaboration is often of crucial importance for being able to participate in the front of international research. The discovery of dishonesty linked to the use of such registers may weaken the global research communities’ interest in collaborating with Nordic researchers.

Research is by nature truth seeking and critical, and has an important task in questioning “established” truths. It is also incumbent on the researcher community to ensure that research activities take place within ethical and honest norms at all times. When dishonest conduct is discovered, the increased focus on norms and the practice of professional ethics provides an opportunity for a renewed discussion of the following up at all levels of research. This case becomes an “eye-opener” which may contribute to an enhanced concentration on the prevention of dishonesty. Even if rules and guidelines for ethical and honest research conduct exist, there is a need for continuous focus on these questions, not least in the researcher education.

The Commission has difficulties in having clear conceptions of whether this case specifically will harm the reputation of Rikshospitalet/Radiumhospitalet MC and the University of Oslo, but the names of these institutions, in particular the first mentioned, will inevitably be linked to Jon Sudbø. It will probably be necessary to allocate resources to show increased openness relating to the practicing of guidelines and quality assurance routines in order to restore and maintain trust. An effort to explain away what has happened will easily be contra productive as regards regaining the trust of the population and authorities. Most people understand and accept that errors and failures can occur now and then.
6.2 Possible harmful consequences regarding the treatment of patients, etc.

The results from the studies have probably been used by many researchers in their works. When the findings referred to are based on incorrect and misleading data, this has in the best of cases caused much wasted work and resources.

Many of the publications deal with the use of diagnostic methods to determine oral cancer and to discuss prognoses for treatment in relation to the time of diagnosis. This may have consequences for the follow-up and treatment of patients. The Commission has not understood it to be its task to discover specific harmful effects. The Commission is aware that this will be a subject for the Board of Health’s own investigation.

However, the Commission is aware that the results have been used in discussions on the value of medicines, also as documentation in discussions about retraction of medicines. Also here, the results of Sudbø’s research may have had negative consequences, both for the treatment of patients and for the use and sales of medicines. Moreover, the Commission has registered that there are reports in the media that Sudbø’s research results have influenced the diagnosis and treatment of certain persons with white patches in their oral cavities in Germany, the UK and the USA. It is also reported in Norwegian media that individual patients have omitted to use painkilling tablets, and rather chosen to live with pain, because it appears from the Lancet article that the tablets entailed an increased risk of cardiovascular diseases, etc.

Evidently, these are very serious matters, and this obvious danger of misleading patients, health staff and researchers with ensuing disadvantages and harmful effects, must have been evident to Jon Sudbø.
7. Criticizable circumstances

7.1 Introductory remarks

In line with its terms of reference, the Commission in this chapter will make a summary of what it found to be criticizable circumstances. For a detailed description of facts and the Commission’s evaluation of Jon Sudbø’s research, see Chapters 4 to 6. The criticizable circumstances the Commission has discovered are related partly to physical persons and partly to institutions.

The Commission’s investigation entailed that 60 authors of scientific publications and several employees at the institutions in fact have been subject to investigation. Regarding individual persons, the Commission, in line with what is stated in Chapter 2, has applied a relatively high threshold for the circumstances that are to form the basis for criticism of individuals, namely gross and serious breaches of good research ethics perpetrated with intent or gross negligence.

The Commission has not found any grounds for believing that other individuals than Jon Sudbø have contributed to the fabrication of data or committed similar gross and serious breaches of regulations either intentionally or with gross negligence. However, Sudbø’s supervisor and most important partner, Albrecht Reith, must suffer a certain criticism for lack of due care.

The fact that the threshold for criticism of individuals is so high, means that few individuals are subject to direct criticism by the Commission. The investigation has disclosed several less gross and serious cases of failing to comply with authorship criteria and the handling of patient data contrary to regulations which, per se, could have given grounds for criticism against more individuals. As mentioned in Chapter 2, however, such an investigation of less serious circumstances would have become disproportionately demanding. Less gross deviations are also serious to research, in particular if seen in connection (collective and cumulative errors). They are a threat to the quality of research and the population’s trust in research. On this background, the Commission has chosen to identify less gross, but nevertheless serious criticizable circumstances, on a more general basis, without mentioning individual persons by name. As accounted for in the introduction, the Commission has chosen to concentrate its investigation on gross breaches of good research ethics, and therefore it does not have a sufficient basis for naming individuals as regards less serious, but nevertheless criticizable circumstances. Moreover, the errors concerned seem to have a certain general incidence, i.e. that the criticism is more related to systems rather than individuals since the deviations to a certain degree must have been known to and therefore apparently accepted by management. The Commission is of the opinion that identifying individuals in such a situation easily will give a distorted impression. As the Commission sees it, it is the duty of the institutions to ensure an appropriate training, organization and monitoring of the institution’s activities, including the research activity. It must be an unconditional requirement that statutes,
regulations and work instructions are made known among the employees and that a certain regular monitoring that the rules are in fact complied with is maintained. In the Commission’s opinion this would imply simple measures which would not be very cost demanding for the management and not very invasive to the researchers. It should be noted here that an evident improvement of these circumstances has occurred over the last years. The Commission will present more specific suggestions for development measures in Chapter 8.

Where criticism of institutions is concerned, the threshold for critical remarks is thus set considerably lower, both in relation to the gravity and the standard of proof of breaches. As regards the “system criticism” the Commission has elected to voice the impressions that it is left with, although the impressions are based on an incomplete and therefore more uncertain basis. The appointing bodies have, as opposed to individual persons, not been given the opportunity to respond to this criticism either. The Commission will nevertheless point at some systematic errors and flaws, because research institutions, and not only those directly involved, probably have a few things to learn from this case and the circumstances disclosed in its wake.

It is the Commission’s hope that the institutional criticism will be perceived as constructive measures for improvement which may enhance the quality and trust in research in the long term.

7.2 Criticism of individual persons

7.2.1 Jon Sudbø

Based on the facts it has found to exist and accounted for in Chapter 4 and the assessments accounted for in Chapters 5 and 6, the Commission finds that Jon Sudbø has broken a series of rules. Most of these breaches have been committed with intent or gross negligence, and without doubt form the basis for criticism and the term scientific dishonesty. The breaches of rules must be seen in context. They occurred systematically from the end of the 1990’s and up to the dishonesty was discovered in January 2006.

As accounted for in section 2.4.5, Sudbø has been allowed to read two draft reports with documentation annexed, among other things. He submitted a series of suggestions to the first draft, but refrained from commenting the revised draft he was subsequently sent. The Commission has considered Sudbø’s suggestions and taken them into account to the extent it found grounds to do so. Apart from one admitted case of fabrication of data in connection with the Lancet article, and some minor admissions regarding two other articles, Sudbø is in all essentials uncomprehending to the fact that the Commission has found that the extent of scientific dishonesty is far more widespread.

In summary, this concerns the following circumstances:
• Manipulation and fabrication of data which form the basis for the PhD dissertation and which form the basis for 13 scientific publications which now must be retracted, see section 4.2-4.4.
• Manipulation and fabrication of data which form the basis for an article in Journal of Clinical Oncology 2005, see section 4.4.
• Manipulation and fabrication of data which form the basis for an article in The Lancet in 2005, see section 4.4.
• Failing to comply with the duty to submit to the Regional Ethical Committee and for a licence from the Data Inspectorate. Unlawful dealing with and access to sensitive patient data, i.e. lack of participants’ consent and/or dispensation from the duty of secrecy from the Norwegian Board of Health (now: the Directorate for Health and Social Affairs), see section 4.2.4.
• Obvious erroneous information and misleading information in publications. For example, it is alleged that the histologic classification was made by four independent pathologists, that the ploidy analysis was performed by four observers, that patients had been included in an annual systemized follow-up project, that patients were included in smoking cessation projects and the like, see in particular section 4.2.
• Intentional misrepresentation in connection with an application for financial support from the National Cancer Institute (NCI), see in particular section 5.3.
• Breach of good scientific practice for including and excluding authors in publications. Co-authors have been abused and misled, see in particular sections 5.2 and 5.3.
• Misleading of sponsors and his employer and others who have provided financial support to Jon Sudbø and his research, including in particular the Cancer Society, Health and Rehabilitation and the Radiumhospitalet, see Chapter 4 to 6.
• Misleading of his own PhD candidate who was given data material which partly was based on fabricated data from Jon Sudbø as the main supervisor. The consequence of this is that the candidate has spent several years on a project which recently was completed, but which now must be retracted. The candidate is probably put back at least two years in time in relation to a possible presentation of a doctoral thesis, see in particular section 4.2.
• Harming the reputation of research. The Commission here refers to the risk of harm to the trust in research in general caused by the dishonest activities, see section 6.1.
• Jeopardizing patients’ safety. Dishonesty in connection with this type of medical research is particularly serious because it entails an obvious danger that the invalid research results will mislead patients, health staff and researchers. This risk must have been obvious to Jon Sudbø. Although the Commission has not seen it as its task to pursue this, it is reasonable to assume that the dishonest
research has had unfortunate and harmful consequences for the diagnosis and treatment of individual patients, see in more detail section 6.2.

7.2.2 Albrecht Reith

The Commission has found grounds for criticism against Professor Albrecht Reith MD at the Rikshospitalet/Radiumhospitalet MC in relation to certain circumstances. This is primarily related to Reith’s role as Jon Sudbø’s PhD supervisor and subsequent primary collaboration partner. In the Commission’s opinion, generally a supervisor is responsible for guiding and monitoring his/her research fellow. The Commission has found that Reith to a certain extent has failed as a supervisor by inadequate following up. This has been a contributing factor to Jon Sudbø having been able to act in contravention of good scientific practice.

The Commission has not found grounds to state that these errors were committed with intent or gross negligence or that Reith is guilty of so-called scientific dishonesty. The Commission has found it to be proven that Reith in some cases should have acted differently, and that he is to blame for not doing so. Thus, it is a question of ordinary negligence. It seems as if Reith had boundless trust in Sudbø. The Commission finds reason to comment that Reith has been highly cooperative in connection with the investigation.

Reith has been allowed to read two drafts of the report and he has submitted comments to certain factual matters. The Commission has considered and taken into account these comments as far as the Commission has found grounds for doing so. Reith has not raised objections to the criticism stated.

In summary, the Commission would in particular emphasize the following circumstances as criticizable:

- Insufficient supervision and due care in relation to obtaining necessary advance evaluations and permissions from the Regional Committee for Medical Research Ethics, the Data Inspectorate and the Board of Health (now: the Directorate for Health and Social Affairs).
- Insufficient supervision and due care in relation to the handling of patient information subject to secrecy.
- Insufficient supervision and due care in relation to the practicing of general principles for authorship. Reference is here made to the fact that several authors brought up Jon Sudbø’s unusual and unlawful practicing of authorship directly with Reith, who apparently did not see reason to follow up and correct this practice. On the contrary, it is the Commission’s impression that Reith protected Sudbø and prevented a further investigation of accusations of unacceptable practice.
- Insufficient due care relating to several publications, in which a series of errors appear. As main supervisor and last author, Reith should have reacted to at least some of these errors. This concerns i.a. the
statement that four independent pathologists had reclassified the entire raw material for the oral
cancer project, and that four independent observers had evaluated the ploidy analyses.

7.3 Criticism of institutions

7.3.1 The Rikshospitalet – Radiumhospitalet MC

The Commission has found reason to criticize the Rikshospitalet/Radiumhospitalet MC represented by its
general management regarding a series of circumstances. The Commission’s basis is that Sudbø during his
entire scientific career primarily was associated with the Radiumhospitalet, which then had the overall
everyday responsibility for his research which was performed under the auspices of the Radiumhospitalet, cf
section 4.2. It should be noted that prior to January 1, 2002, the State represented by the Ministry of Health,
was responsible for the Radiumhospitalet. As from and including January 1, 2002, the Radiumhospitalet
became a separate medical center and thus a separate legal entity. As from and including January 1, 2005, the
Rikshospitalet MC and the Radiumhospitalet MC were merged into one medical center and legal entity: The
Rikshospitalet – Radiumhospitalet MC. The medical center has not been given the opportunity to respond to
this criticism, cf section 2.4.6.

In introduction, the Commission would emphasize that this criticism is not based on comprehensive
investigations of the management, but rather on more or less clear impressions which the Commission is left
with after investigating a specific personnel matter. The Commission nevertheless finds reason to mention
these impressions.

When a research institution, which the MC is, makes provisions for research at the institution, it must
be prepared to carry the full responsibility for the individual researcher and the relevant research project,
regardless of whether others also have an independent responsibility. Patients and others who relate to the
MC, including collaborating institutions, must be able to expect that researchers at the MC work on behalf of
the same MC, and that the MC has the overall responsibility.

The medical center must therefore suffer criticism for what appears as inadequate training,
management and control of Jon Sudbo’s and other employees’ research activities at the institution. This has
probably been a contributing factor to the dishonest research being able to take place and be carried on for
such a relatively long time.

Several researchers at the institution have described situations from earlier periods which in the
Commission’s opinion indicate a disturbing lack of awareness of the prevailing rules for good research
practice. This applies in particular to rules on secrecy, protection of personal data, authorship and advance
assessments of research projects which are the rules which have been particularly relevant in this case.
Furthermore, the distribution of responsibility regarding the institution’s research have been unclear
and too much of the activity has been left to the individual researcher. Unacceptable matters which in fact were pointed out, and which could have brought the dishonest research to light, were not followed up and managed in a satisfactory way.

Here should be noted that there is no lack of good intentions. The management has had a very clear attitude as regards its own responsibility and high expectations to its own employees. In conversations with the Commission, the management referred to internal work instructions and other measures as for example the so-called Protocol Committee and coordinating office for research, which is meant to contribute to the implementation of rules and regulations and enhanced research practice. The management also had a very clear attitude regarding expectations that the employees comply with all statutes, regulations and work instructions, including the Helsinki Declaration as well as the Vancouver Rules. However, the Commission is left with an impression that these measures have not been followed up well enough. By this, an attitude among the employees has been allowed to develop to the effect that after all it did not matter so much with for example the duty of secrecy, recommendations from the Regional Committee for Medical Research Ethics and practicing of the authorship criteria. Several people stated to the Commission that the Vancouver Rules are not binding for them – they are only guidelines, whereas the management stated that they evidently enough are binding on their employees. The management must assume the responsibility for this discrepancy and confusion.

The Commission has the impression that circumstances have become/are becoming better. Insufficient follow up of research by management was hardly an unusual phenomenon at some Norwegian research institutions some years ago. Traditionally, researchers have worked very freely, both at universities and Norwegian hospitals. Clinicians have been encouraged to carry on research, but sufficient awareness related to the different roles and partly different requirements put to them has probably not been sufficient, neither on the part of researchers nor management. Insufficient and failing routines, and an insufficient system for notifying irregularities, have been an unfortunate combination for the Radiumhospitalet. The medical research community is thus in a transition phase as regards the organization and formalities relating to medical research. The Commission believes that this specific case has been an eye-opener for this as well as for other research institutions, and will probably contribute to speeding up this development process.

The Commission nevertheless finds reason to maintain the criticism of the Rikshospitalet/Radiumhospitalet MC. The criticizable circumstances can be summarized as:

- Insufficient advance control and organization of Sudbø’s PhD project, including specification of distribution of responsibility.

- Insufficient training and consciousness-raising of Sudbø and other employees about the rules for handling patient material, advance assessment of research projects and authorship.
• Insufficient management and routines for discovering and handling deviations from internal instructions, etc.

7.3.2 The University of Oslo – The Odontology

The Commission finds reason to level a certain criticism against the University of Oslo, the Faculty of Odontology, for delivering patient material and data from the Odontology to Jon Sudbø and Albrecht Reith without the existence of participant’s consents or dispensations from the duty of secrecy as required at that time, cf section 4.2.7, cf section 4.2.4. The delivery of data therefore appears as a breach of the regulations in force at that time. The University of Oslo has not been given the opportunity to respond to this criticism, cf section 2.4.6.

In this context is noted that Jon Sudbø was employed in a 20% position only at the University of Oslo from May 2, 2005 until the beginning of 2006 and also that the University during this period had a more secondary general responsibility for Jon Sudbø’s research activities, compared with the Rikshospitalet/Radiumhospitalet MC.

7.3.3 The University of Bergen – Gade’s Institute

The Commission has found reason to level a certain criticism against the University of Bergen, Department of Pathology, “Gade’s Institute”, for not having made sure that Jon Sudbø and Albrecht Reith had obtained consent from the patients or dispensation from the duty of secrecy when patient material and data were delivered to them, cf section 4.2.7, cf section 4.2.4. The delivery of data thus appears as a breach of the regulations in force at that time. The University of Bergen has not commented on the Commission’s draft of criticism.

7.3.4 The Cancer Registry

The Commission considered whether there was reason to level a certain criticism against the Cancer Registry for not having made sure that Jon Sudbø and Albrecht Reith had obtained consent from the patients or dispensation from the duty of secrecy when cancer registry data connected to their patient data in 1996 were delivered to them, cf section 4.2.7, cf section 4.2.4. The framework concession of December 9, 1985, item 4.3 no. 2, third dash line, states that the delivery of information for research purposes was conditional on observance of the rules on secrecy, where appropriate after dispensation. No dispensation for the relevant delivery was granted.

The Cancer Registry was notified that the Commission considered to level a certain criticism on this basis and made use of its right to comment on an earlier draft of section 7.3.4 of the report. In a letter to the Commission dated June 20, 2006, the Cancer Registry asserted that the draft criticism is based on an erroneous conception of the Cancer Registry’s different roles. The Cancer Registry asserts that it understood Jon Sudbø’s request of February 20, 1996, as a routine request for follow-up data for patients at the
Radiumhospitalet, Department of Pathology, which did not require advance permission, such as for example dispensation from the duty of secrecy, see in more detail section 4.2.7.

The Commission has considered the Cancer Registry’s comments and compared them with the information given in Jon Sudbø’s letter of February 20, 1996 to the Cancer Registry, quoted in section 4.2.7, and other information in the case. On that background, the Commission finds that it appears from the letter that it is a question of a research project, something which the Cancer Registry should have understood. The delivery of data then appears as a breach of the licence conditions.

7.4 General remarks
As mentioned, the Commission has investigated all 60 coauthors. The Commission has reviewed the role of the individual coauthor to see if anyone may be suspected of having participated in the fabrication of research data or other gross breaches of good scientific practice. The Commission has found that there are no reasons to believe that other persons than Jon Sudbø, either intentionally or with gross negligence, have contributed to the fabrication of data or committed similar gross and serious breaches of good scientific practice.

For general deterrence reasons, among other things, the Commission has nevertheless found reason to point out certain criticizable circumstances on a more general basis. The Commission has difficulty in understanding that the breaches of good scientific practice which have been discovered, probably have been ongoing for such a comparatively long period without anyone discovering it. In Chapter 5, the Commission touched upon how this may have happened. Obviously, Jon Sudbø had the main responsibility for the articles of which he was the first author. He had full control over the raw data and the analyses made. Moreover, he had full control over who was a coauthor and who was not. By this, he was able to distribute the work such that the different contributors/coauthors did not have much access to the other contributors/coauthors’ actual tasks and contributions. By this distribution of tasks, the coauthors have been deceived by only having been involved to a rather restricted degree. At the same time, they were involved in such a way that they “nevertheless” accepted the authorship. Admittedly, several of them expressed doubt about whether they should take part as coauthor, and brought this up with Jon Sudbø and Albrecht Reith. Some even pointed out that the coauthor practice followed by Jon Sudbø was unacceptable, and made this clear to Jon Sudbø and Albrecht Reith. They were then told that this view was taken note of and that it should not happen again. No improvement took place, however. These authors were instead excluded from further collaboration.

In retrospect it is obvious that many persons ought to have become suspicious, reacted more strongly and investigated matters more closely. In this context, several persons have had occasion to notify the
management of the institution. There were also several persons in the medical community who were suspicious and skeptical to Jon Sudbø’s research and pointed this out to Jon Sudbø as well as Albrecht Reith and the management at the Radiumhospitalet. However, no proper routines for notification existed, and criticism against Jon Sudbø was brushed aside, explained away and petered out. In fact, several persons have stated to the Commission that they did not want to end up in a whistleblower position, and for that reason refrained from making further investigations. They maintain that ending up in the position of a whistleblower would be a great personal burden for them, in particular when a researcher who had a sort of status as the community’s “favorite son” was involved.

The reason that the Commission has not chosen to make a more detailed and thorough investigation of individual persons for less serious breaches of good scientific practice is also that the Commission understands that the practicing of authorship criteria is hardly unique to this case.

Several coauthors have been listed without their knowledge. Some of them became aware of such listings after publication and brought up this unacceptable practice with Jon Sudbø without any ensuing consequences. These circumstances could and should have been reported to the management, providing the management with an opportunity to take action on a more principal basis. A general characteristic seems to be that many of the coauthors did not have a very conscious relationship to the responsibility inherent in being listed as a coauthor of a scientific publication. In other words, they have taken this role and responsibility too lightly.

The media has devoted much attention to the fact that Jon Sudbø’s co-habitant, Wanja Kildal, and his brother, Asle Sudbø, were coauthors in several publications. For that reason the Commission will, in conclusion, remark that both of them collaborated with the Commission and contributed to illuminating the case. Having account to the extensive media focus, with its inherent suspicions directed against these two persons, the Commission finds reason to underline that the investigation has not disclosed any grounds for believing that any of them have been guilty in or contributed to scientific dishonesty.
8. Recommendations

8.1. The institutions

As accounted for in Chapter 5, the Commission is of the opinion that the breaches of good scientific practice which have been disclosed, can hardly be explained by a lack of research-ethical rules and principles. Nor can they be explained solely by reference to a single dishonest researcher. The interaction of a series of unfortunate circumstances has played a role in this case. On this background, the Commission has elected to emphasize the research communities, and in particular the research institution’s, joint responsibility to promote honest and ethically proper research of a good quality.

The Commission considers it to be outside its terms of reference to submit detailed suggestions as to how improvements of internal institutional control routines and the organization of research should be implemented. However, the Commission will point out some circumstances of a more general nature, which may prove effective and relatively simple to implement:

*Institutional implementation of the prevailing set of rules*

Research institutions must to a larger extent make all researchers and supervisors aware of the prevailing rules and the liability attached to to breaches of the rules. Ensuring that applicable statutes and rules and regulations are complied with and enforced is to a large degree an institutional system and management responsibility, where, in the Commission’s opinion, there is an evident potential for improvement. For example, the responsible research institution must have a satisfactory overview of and exercise satisfactory control over all research projects taking place at, or under the auspices of, such institution, without it necessarily being in conflict with academic freedom. The need for preventive work, and the research institutions’ responsibility for development of environments which take care of lifelong learning within the scope of research ethics and good research practice, is also emphasized in the preparatory works to the newly enacted Research Ethics Act (not yet in force). For example, the institutions could have been more explicit regarding whether and to what extent the Vancouver Rules are to be considered as binding for their employees. The Commission would also here refer to the simple but good advice to be found in *Guidelines for the implementation of research projects related to medicine and health* (Annex 5).
Handling of data and ethical evaluation of projects

As a minimum, the institutions should have routines to ensure that necessary permits for research involving people, human biological material, personal data information and/or animals are in place when research projects are initiated. In addition, the universities should require documentation that these are in place when PhD dissertations are submitted, for example.

Filing of research data

The research institutions should create systems taking care of the filing and storing of research data, as, i.a., the Research Council requires when funds are granted.

The contents of the supervisor role

The content of the supervisor role must be made more explicit, and a more precise responsibility should be imposed on the supervisor to ensure that research-ethical factors are understood.

Notification of errors and flaws

Better arrangements for notification of errors and flaws should also be implemented, for example by the creation of a researcher ombudsman, as suggested by some.

8.2 The journals

In the Commission’s opinion, this case has disclosed certain weaknesses in the routines practiced in connection with the publication of medical research articles. The Commission believes that, in order to contribute to the proper compliance with prevailing rules, medical journals should introduce and practice a system in which all coauthors are made part of the communication with the journals. They should be sent letters informing them that they have been stated as coauthors, and they should individually submit their confirmations of this directly to the respective editors. At the same time, the authors should submit a written account of what their intellectual contribution to the work consists of, which is something some journals require already. Likewise, the Commission believes that it would be reasonable that all coauthors are sent review statements. In this way the individual author’s awareness of his/her responsibility would be strengthened, and one would also avoid that researchers are listed as authors without any knowledge of this fact.

If such principles had been applied to the Lancet article, it is, in the Commission’s opinion, fairly likely that the research fraud would have been discovered already prior to publication, in particular considering fairly negative statements and critical questions by one of the professional colleagues who
reviewed the articles. Corresponding principles should apply to contributors who are listed under acknowledgements.

With the use of modern electronic communications, these suggestions for changed routines ought not to imply substantial administrative or financial burdens, in the Commission’s opinion. In order to alleviate the administrative challenges, one should therefore require that the submission of manuscripts be accompanied by a list of the email addresses of all authors/coauthors and contributors.

Furthermore, the Commission has considered whether the system of “fast-track publishing” which is practiced by some journals, may have unfortunate effects, in the sense that there is too little time between the evaluation by professional colleagues and publication for professional objections to the work to form part of the procedure. The Commission here confines itself to pointing at the problem. Even though the persons who are employed as professional colleagues in a “fast track” review system possess solid professional weight and integrity, one can nevertheless not entirely disregard that the time pressure inherent in the system itself generates an unnecessary risk that errors are not discovered.

8.3 The Commission’s concluding remark

In conclusion, the Commission will remark that although this case has been very serious and tragic for individuals, institutions and Norwegian research more generally, there appears to be a remarkable will internally in the research community to turn the case around to something positive – something everyone can learn from. Frequent contributions to newspapers, debates and seminars have shown an already great involvement in many research environments. The Commission will support such a way of thinking, and at the same time caution against sweeping this extraordinary case under the carpet – because it is extraordinary – and just continue as before.

On the contrary, this case provides an opportunity for a thorough discussion of different sides of the norms related to good research practice. The research community must make an all-out effort to make plain research’s traditional ideals of honesty, thoroughness, trustworthiness and openness. And this must be made visible to the general public so that the population’s trust in Norwegian research is maintained and reinforced.
Annexes
Annex 1: Jon Sudbø’s publication list


## Annex 2: Evolvement of the authorship criteria

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med. 1997 Jan 23;336(4):309-15. <strong>Authorship</strong> All persons designated as authors should qualify for authorship. Each author should have participated sufficiently in the work to take public responsibility for the content. Authorship credit should be based only on substantial contributions to (a) conception and design, or analysis and interpretation of data; and to (b) drafting the article or revising it critically for important intellectual content; and on (c) final approval of the version to be published. Conditions (a), (b), and (c) must all be met. Participation solely in the acquisition of funding or the collection of data does not justify authorship. General supervision of the research group is not sufficient for authorship. Any part of an article critical to its main conclusions must be the responsibility of at least one author. Editors may ask authors to describe what each contributed; this information may be published. Increasingly, multicenter trials are attributed to a corporate author. All members of the group who are named as authors, either in the authorship position below the title or in a footnote, should fully meet the above criteria for authorship. Group members who do not meet these criteria should be listed, with their permission, in the Acknowledgments or in an appendix (see Acknowledgments). The order of authorship should be a joint decision of the coauthors. Because the order is assigned in different ways, its meaning cannot be inferred accurately unless it is stated by the authors. Authors may wish to explain the order of authorship in a footnote. In deciding on the order, authors should be aware that many journals limit the number of authors listed in the table of contents and that the National Library of Medicine lists in MEDLINE only the first 24 plus the last author when there are more than 25 authors.</td>
</tr>
<tr>
<td>2003</td>
<td>Davidoff F, Godlee F, Hoey Glass R, Overbeke J, Utiger R, Nicholls MG, Horton R, Nylenen M, Hojgaard L, Kotzin S; International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. J Am Osteopath Assoc. 2003 Mar;103(3):137-49. <strong>Authorship</strong> All persons designated as authors should qualify for authorship, and all those who qualify should be listed. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. One or more authors should take responsibility for the integrity of the work as a whole, from inception to published article. Authorship credit should be based only on (1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. Conditions 1, 2, and 3 must all be met. Acquisition of funding, the collection of data, or general supervision of the research group, by themselves, do not justify authorship. Authors should provide a description of what each contributed, and editors should publish that information. All others who contributed to the work who are not authors should be named in the Acknowledgments, and what they did should be described.</td>
</tr>
</tbody>
</table>
Increasingly, authorship of multicenter trials is attributed to a group. All members of the group who are named as authors should fully meet the above criteria for authorship. Group members who do not meet these criteria should be listed, with their permission, in the Acknowledgments or in an appendix (see Acknowledgments, page 140). The order of authorship on the byline should be a joint decision of the coauthors. Authors should be prepared to explain the order in which authors are listed.
### II.A Authorship and Contributorship

#### II.A.1. Byline Authors

An “author” is generally considered to be someone who has made substantive intellectual contributions to a published study, and biomedical authorship continues to have important academic, social, and financial implications.

1. In the past, readers were rarely provided with information about contributions to studies from those listed as authors and in acknowledgments.
2. Some journals now request and publish information about the contributions of each person named as having participated in a submitted study, at least for original research. Editors are strongly encouraged to develop and implement a contributorship policy, as well as a policy on identifying who is responsible for the integrity of the work as a whole. While contributorship and guarantorship policies obviously remove much of the ambiguity surrounding contributions, it leaves unresolved the question of the quantity and quality of contribution that qualify for authorship. The International Committee of Medical Journal Editors has recommended the following criteria for authorship; these criteria are still appropriate for those journals that distinguish authors from other contributors.

- **Authorship credit should be based on**
  1. substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
  2. drafting the article or revising it critically for important intellectual content; and
  3. final approval of the version to be published.

Authors should meet conditions 1, 2, and 3.

- When a large, multi-center group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript.
  These individuals should fully meet the criteria for authorship defined above and editors will ask these individuals to complete journal-specific author and conflict of interest disclosure forms. When submitting a group author manuscript, the corresponding author should clearly indicate the preferred citation and should clearly identify all individual authors as well as the group name. Journals will generally list other members of the group in the acknowledgements. The National Library of Medicine indexes the group name and the names of individuals the group has identified as being directly responsible for the manuscript.

- Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

- All persons designated as authors should qualify for authorship, and all those who qualify should be listed.

- Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Some journals now also request that one or more authors, referred to as “guarantors,” be identified as the persons who take responsibility for the integrity of the work as a whole, from inception to published article, and publish that information. Increasingly, authorship of multi-center trials is attributed to a group. All members of the group who are named as authors should fully meet the above criteria for authorship. The order of authorship on the byline should be a joint decision of the coauthors. Authors should be prepared to explain the order in which authors are listed.
<table>
<thead>
<tr>
<th>Year</th>
<th>Acknowledgments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>At an appropriate place in the article (the title-page footnote or an appendix to the text; see the journal’s requirements) one or more statements should specify (a) contributions that need acknowledging but do not justify authorship, such as general support by a departmental chair; (b) acknowledgments of technical help; (c) acknowledgments of financial and material support, which should specify the nature of the support; and (d) relationships that may pose a conflict of interest. Persons who have contributed intellectually to the paper but whose contributions do not justify authorship may be named and their function or contribution described — for example, “scientific advisor,” “critical review of study proposal,” “data collection,” or “participation in clinical trial.” Such persons must have given their permission to be named. <strong>Authors are responsible for obtaining written permission from persons acknowledged by name, because readers may infer their endorsement of the data and conclusions.</strong> Technical help should be acknowledged in a paragraph separate from those acknowledging other contributions.</td>
</tr>
<tr>
<td>2003</td>
<td>List all contributors who do not meet the criteria for authorship, such as a person who provided purely technical help, writing assistance, or a department chair who provided only general support. Financial and material support should also be acknowledged. Groups of persons who have contributed materially to the paper but whose contributions do not justify authorship may be listed under a heading such as “clinical investigators” or “participating investigators,” and their function or contribution should be described—for example, “served as scientific advisors,” “critically reviewed the study proposal,” “collected data,” or “provided and cared for study patients.” <strong>Because readers may infer their endorsement of the data and conclusions, all persons must have given written permission to be acknowledged.</strong></td>
</tr>
</tbody>
</table>
II.A.2. Contributors Listed in Acknowledgments

All contributors who do not meet the criteria for authorship should be listed in an acknowledgments section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair who provided only general support. Editors should ask authors to disclose whether they had writing assistance and to identify the entity that paid for this assistance. Financial and material support should also be acknowledged. Groups of persons who have contributed materially to the paper but whose contributions do not justify authorship may be listed under a heading such as “clinical investigators” or “participating investigators,” and their function or contribution should be described—for example, “served as scientific advisors,” “critically reviewed the study proposal,” “collected data,” or “provided and cared for study patients.” Because readers may infer their endorsement of the data and conclusions, all persons must give written permission to be acknowledged.
Annex 3: Files and lists which the Commission has used in the investigation of the articles in New England Journal of Medicine 2001 and 2004

<table>
<thead>
<tr>
<th>File name</th>
<th>Records</th>
<th>Note</th>
<th>Source/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Updated rawdata (Excel)</td>
<td>150</td>
<td>First file sent to the US for New England Journal of Medicine 2004</td>
<td>JJL 2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Does not have a link key</td>
<td></td>
</tr>
<tr>
<td>Sudbø8 (Excel)</td>
<td>150</td>
<td>Last file sent to the US for New England Journal of Medicine 2004</td>
<td>JJL 2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Does not have a link key</td>
<td></td>
</tr>
<tr>
<td>Reith paper list (rawdata oral</td>
<td>150</td>
<td>Identical to Sudbø8 on date variables – contains also block numbers</td>
<td>AR 2006</td>
</tr>
<tr>
<td>mucosa)</td>
<td></td>
<td>on 142 records which enables linkage</td>
<td></td>
</tr>
<tr>
<td>L29 (Excel)</td>
<td>147</td>
<td>Contains the same block number as Reith paper list. The heading of</td>
<td>Radiumhospitalet</td>
</tr>
<tr>
<td></td>
<td>records</td>
<td>the list is “Date: April 15, 1998 Main record Jnr L29 Project Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucosa Paraffin Blocks from Haukeland”</td>
<td></td>
</tr>
<tr>
<td>L31 (Excel)</td>
<td>106</td>
<td>Date: April 1998 Main record Jnr L31 Project Oral Mucosa Paraffin</td>
<td>Sent from HD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protease 60min. Hydrolysis 60min</td>
<td></td>
</tr>
<tr>
<td>L34 (Excel)</td>
<td>69</td>
<td>Date: March 8, 1999 Main record Jnr L34 Material: Dysplasia from Fac</td>
<td>Sent from HD</td>
</tr>
<tr>
<td></td>
<td>records</td>
<td>of Odontology. Received blocks, cut 50um + 3 uncolored biopsy samples</td>
<td>2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Method: Monolayer Feulgen colored + color HE of 1 uncolored cut</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Protease 0.5mg/ml for 60 min 37°C. 5N HCl 60min Basic Fuchsin 2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NB! Acc. to agreement with Jon this protocol is excluded. Samples in</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>this series is given L31 October 23, 2001 Tidied in biopsy specimens</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>and blocks. Biopsy specimens not changed to L31. Consequently filed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>under L34. Project responsible: Jon Sudbø Sign.: Date:</td>
<td></td>
</tr>
<tr>
<td>L47 (Excel)</td>
<td>64</td>
<td>Date: March 24, 2000 Main record Jnr L47 Material: Normal mucosa</td>
<td>Sent from RP</td>
</tr>
<tr>
<td></td>
<td>records</td>
<td>Method: monolayer from paraffin-imbedded material 1. One HE cut if</td>
<td>2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>little material, only monolayer to be made 2. nx 50 um biopsy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>specimens 3. One HE2 cut</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Project responsible: Jon Sudbø Sign.: Date:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>December 2000. Project completed delivered to Jon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Date: March 24, 2000 Main journal</td>
<td></td>
</tr>
</tbody>
</table>

49 JJL=J.Jack Lee, AR= Albrecht Reith, JS= Jon Sudbø, HD= Håvard Danielsen, RP=Ruth Punthervold
<table>
<thead>
<tr>
<th>Dataset</th>
<th>Lines/Persons</th>
<th>Description</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ploidy list (Excel)</td>
<td>393 lines in the Excel sheet</td>
<td>File name: All Original blocks and HE biopsy specimens linked to ploidy prep and the L29 series.xls Contains a link between ploidy preparation and block number and link to the L29 series</td>
<td>Produced by RP 2006</td>
</tr>
<tr>
<td>X diagnoses (SPSS)</td>
<td>311 records for 195 persons</td>
<td>All at Dnr-js2 with cancer diagnosis per 2006 (195 of 226 persons)</td>
<td>The Cancer Registry 2006</td>
</tr>
<tr>
<td>X persons (SPSS)</td>
<td>226 persons</td>
<td>All at Dnr-js2 supplemented by p.id.no. and date of death per 2006</td>
<td>The Cancer Registry 2006</td>
</tr>
<tr>
<td>Gade</td>
<td>590 records 162 persons</td>
<td>All referring letters from Gade concerning persons from Dnr-js2</td>
<td>The Cancer Registry 2006</td>
</tr>
<tr>
<td>The Odontology, Oslo</td>
<td>132 records 62 persons</td>
<td>All referring letters from the Odontology, Oslo, concerning persons from Dnr-js2</td>
<td>The Cancer Registry 2006</td>
</tr>
<tr>
<td>Paper list Gade</td>
<td>178 records (block number) 144-146 persons</td>
<td>Received de-identified with block number</td>
<td>Gade 1997</td>
</tr>
</tbody>
</table>
### Annex 4: Table

Raw data linked to information from the Cancer Registry and information on ploidy preparations from the Radium Hospital. Sudbø8 which formed the basis for the article in NEJM 2004 is identical to Raw data which in addition contained prep_no which enabled linkage. Oral cancer is defined by the codes 1400-1499. Bold types shows records in which the date of oral cancer is before the date when the biopsy was taken (date for prep_no). Prep_no is deleted. Missing means that there was no prep_no on the Raw data file.

<table>
<thead>
<tr>
<th>Ptnid</th>
<th>unique persons</th>
<th>Prep_no</th>
<th>Year prep</th>
<th>Year cancer</th>
<th>Oral cancer</th>
<th>Year of death</th>
<th>Year leukoplakia</th>
<th>Year cancer</th>
<th>Link to prep_no</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P1</td>
<td></td>
<td>1981</td>
<td>Yes</td>
<td>1981</td>
<td>1982</td>
<td>Yes</td>
<td></td>
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<td>2</td>
<td>P2</td>
<td></td>
<td>1981</td>
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<tr>
<td>3</td>
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<td></td>
<td>1981</td>
<td>Yes</td>
<td>1983</td>
<td>1986</td>
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<tr>
<td>4</td>
<td>P4</td>
<td></td>
<td>1981</td>
<td>Yes</td>
<td>1991</td>
<td>1993</td>
<td>2000</td>
<td>Yes</td>
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<tr>
<td>6</td>
<td>P6</td>
<td></td>
<td>1981</td>
<td>Yes</td>
<td>1986</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>P7</td>
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<td>No</td>
<td>1993</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>8</td>
<td>P8</td>
<td></td>
<td>1980</td>
<td>Yes</td>
<td>1983</td>
<td>1993</td>
<td></td>
<td>Yes</td>
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</tr>
<tr>
<td>10</td>
<td>P10</td>
<td></td>
<td>1982</td>
<td>No</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>P11</td>
<td></td>
<td>1973</td>
<td>No</td>
<td>1983</td>
<td>1990</td>
<td></td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>P12</td>
<td></td>
<td>1982</td>
<td>Yes</td>
<td>1983</td>
<td>1994</td>
<td></td>
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<td>13</td>
<td>P13</td>
<td></td>
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<td>Yes</td>
<td>1984</td>
<td>1992</td>
<td></td>
<td></td>
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<tr>
<td>14</td>
<td>P14</td>
<td></td>
<td>1982</td>
<td>No</td>
<td>1983</td>
<td>1994</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>P15</td>
<td></td>
<td>1976</td>
<td>Yes</td>
<td>1983</td>
<td>1990</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>P16</td>
<td></td>
<td>1982</td>
<td>Yes</td>
<td>1992</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>P17</td>
<td></td>
<td>1987</td>
<td>Yes</td>
<td>1991</td>
<td>1993</td>
<td></td>
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<tr>
<td>18</td>
<td>P18</td>
<td></td>
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Annex 5: The Dishonesty Committee’s Guidelines

The Research Council of Norway 2001

Guidelines for the implementation of research projects related to medicine and health

Objective of the guidelines: To provide advice about the design of research plans, documentation and data storage in relation to medical and health research. The objective is to prevent disagreements between project participants and to prevent doubts from being raised about the implementation of a project.

Pre-project checklist:

- Formulate the project’s purpose and objectives clearly. Make a project plan (research protocol) which includes what you want to record (effects, variables), how you want to perform the project (method) and the materials and procedures you intend to use.
- Identify any mutuality or conflicts of interest related to the project or among the participants.
- Agree on who is in charge of the project and on the division of labor.
- Agree on who will be writing any publications that are planned. If the situation changes during the project, make a new agreement.
- Clarify questions involving the ownership and user rights to any original data or processed results.
- Any project that includes trials on humans must be submitted to the Regional Research Ethics Committee for Medicine (REK) for approval prior to initiation. Such projects require the informed consent of the subjects in the sample. Draw up your inclusion and exclusion criteria, as well as your criteria for aborting the project. Secure permits for data storage, confidentiality and other relevant conditions, where so required.
- Experiments on animals must be submitted to and approved by the Norwegian Animal Research Authority (NARA) prior to initiation.
- Document equipment that performs measurement-related functions and other measurement instruments, and establish routines for control, calibration and validation.

Please note that these guidelines are neither entirely up to date nor exhaustive, and that more recent legislation, as for example the Bio Bank Act that came into force in the summer of 2003 is not included.
• Make experiment plans and appurtenant registration forms accessible, straightforward, unambiguous and comprehensible to all those involved in the project. Prepare this material far enough in advance to allow adequate time for training, and possibly for testing and adjustment.

**While the project is in progress:**

• All parties involved in a project have a mutual obligation to provide information about progress, results, processing, presentation and interpretation.

• Document any deviations from the original investigative plan and experiment procedures. Be sure that any changes in the project or in the potential consequences of any changes are approved by project management.

• Ensure that data on individuals gathered during the course of clinical research projects can be identified and recovered for each individual test subject according to the terms and conditions laid down by the relevant control agency/authorities. The documentation must specify who has collected the data, and when it was collected.

• Ensure that equipment used for measurement is checked and calibrated on a regular basis. The documentation must specify who have checked the equipment, and when.

• Ensure that the materials (e.g. chemicals, preparations, materials) to be used in the project can be identified and documented.

**Post-project follow-up:**

• Organize original data systematically, safely and so that it is readily recoverable. Pursuant to the national statutory provisions that apply at any given time, licensing terms, contractual terms and conditions, and institution-specific regulations, data, including consent forms, must ordinarily be kept for at least 10 years. The same applies to plans for studies, receipts and descriptions of deviations, if any.

• Once a project is completed, the information may be stored collectively in institutions approved for this purpose. Be sure to sign a final agreement regarding future ownership, storage rights and user rights to data and other material made available as a result of the project. Be especially careful when it comes to person-specific data in order to avoid conflicts related to agreements with the human subjects involved.

If necessary, the owner of the data should be able to establish traceability from published composite data, e.g. tables and figures, to original data.
Medical words and expressions\textsuperscript{51}

\textit{Adenoma}: a benign tumor emanating from and partly structured as a gland

\textit{Biopsy}: a tissue sample from a living patient for microscope examination

\textit{Carcinoma in situ}: term for cellular changes that indicate a beginning cancer development without spreading having yet started, a precursor of cancer

\textit{Diploid}: denoting that a cell contains two sets of chromosomes

\textit{DNA aneuploidy}: cells with deviating DNA amount, may be found in many malignant tumors

\textit{DNA histogram}: Graphical presentation of analysis results for DNA amount used in ploidy classification (see separate explanation)

\textit{Dysplasia (mild, moderate or severe)}: a growth abnormality, incomplete of erroneous development of bones, cartilage and/or skin

\textit{Erythroplakia}: Red patches (plaques) or lesion in the oral mucosa (also called dysplastic leukoplakia); the lesion is related to leukoplakia, but more rare and more serious as it more frequently develops into cancer

\textit{Graph theory}: Analysis and numerical representation of graphical presentations

\textit{Histopathology}: The study of pathological changes in tissues

\textit{Hydrolysis and Feulgen coloring}: Techniques used for the preparation of tissue preparations

\textit{Carcinoma}: a malignant tumor in epithelial tissues, i.e. in skin, mucosa or glands

\textit{Chemoprevention}: a term used in particular for intake of various substances to prevent the development of cancer

\textsuperscript{51}Mainly taken from: Nylenna M. Medisinsk ordbok [Medical Dictionary]. Oslo: Kunnskapsforlaget, 2005.
**Colorectal cancer:** Cancer of the large intestine and rectum

**Lesion:** generic term for circumscribed injuries to the body

**Leukoplakia:** white patches (plaque) in the oral mucosa that cannot be scraped away, the leukoplakia may develop into cancer

**Malignant:** cancerous

**Malign transformation potential:** a lesion with a high malign transformation potential (e.g. erythroplakia) more frequently develops into cancer than a lesion with a lower malign transformation potential (e.g. leukoplakia)

**Melanoma:** birth mark cancer, pigment cell cancer

**NSAID:** Non steroidal anti-inflammatory drugs

**Odontology:** Dental medicine

**Oral:** Belonging or pertinent to the mouth

**Squamous cell carcinoma:** Malignant tumor developed from squamous cells in the skin or mucosa

**Ploidy classification:** the classification of DNA amount as diploid, tetraploid or aneuploid (see separate explanations)

**Premalign illnesses:** Conditions that may develop into cancer

**Re-classification:** Repeated classification

**Referring letter:** a letter from a physician to another physician, hospital, laboratory or the like asking for further care or examination

**Tetraploid:** Having four sets of chromosomes in the cell nucleus
**Tissue block**: Paraffin-embedded tissue used for making histological biopsy specimens.
## Statutes and regulations referenced in the report

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**Repealed acts**

| Act relating to Personal Data Filing Systems | Lov om personregistre m.m. (LOV 1978-06-09-48). |
| Act relating to dentists | Lov om tannleger (LOV 1980-06-13 nr 43). |
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Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication – updated February 2006