

To whom it may concern

Copenhagen, 2 January 2014

Brief background information

On 18 December 2013, the Danish Committees on Scientific Dishonesty (DCSD) published their decision on three complaints, all of which have to do with the undersigned. I submitted one of the three complaints myself on 2 April 2011, against Milena Penkowa for image manipulation in four articles. In this case, the DCSD found that my complaint was justified. The second complaint, claiming scientific misconduct, was submitted by Professor Jamie Timmons on 18 April 2011 against me and a number of colleagues. This case was rejected by the DCSD. The third complaint was submitted by Professor Henrik Galbo against me on 19 July 2011, claiming scientific dishonesty in twelve articles. The DCSD's conclusion was that there had been scientific dishonesty in six of the articles. The decision can be read in full at <http://fivu.dk/forskning-og-innovation/rad-og-udvalg/udvalgene-vedrorende-videnskabelig-uredelighed/afgoelser/2013/anonymiseret-afgoelse-af-18-december-2013-sag-nr-2.pdf>.

Before the final decision was issued, the DCSD published a preliminary draft decision in June 2013 to which the media were also given full access in its entirety. The preliminary draft decision and my response are available at:

<http://www.forskeren.dk/wp-content/uploads/Udkast-til-afgoelse-i-UVVU-sag.pdf>

http://universitetsavisen.dk/files/universitetsavisen.dk/uvvu_1_juridisk_del.pdf

http://universitetsavisen.dk/files/universitetsavisen.dk/uvvu_2_faglig_del_afsluttende_bemaerkninger.pdf

General information on the complaints

Two and a half years in the making, the DCSD's decisions have engendered a great deal of comment in the media and discussion in the scientific community, both in Denmark and Internationally. I have repeatedly apologised for not having discovered the image manipulations carried out by Milena Penkowa, and I have also apologised for the unintended errors in some articles and subsequently taken it upon myself to correct them. I stand by my apologies.

However, it remains my view that there is a crucial difference between cheating and making unintentional mistakes, which is why I have emphasized that the errors pointed to were of a nature that could not be considered comparable with dishonesty.

As a result, I looked forward to the decision of 18 December, because it meant the end of a drawn-out process, as the DCSD's decision cannot be appealed and must thus be considered final. In view of the length of the process and all the resources expended on clarifying these complaints, one would expect the final decision to be correct and irrefutable.

Unfortunately, this is not the case, as there are both formal and specific factual errors in the decision that could have been avoided.

The DCSD decision dated 18 December 2013 differs greatly from the June 2013 preliminary draft decision. A number of matters labelled misconduct in the draft have been withdrawn, but I am now being judged on the basis of charges, which were not submitted for my consideration and to which I have not had the opportunity to respond. This is objectionable because the DCSD are also guilty of misunderstandings and

errors that could have been avoided, had I had the opportunity to appear before the DCSD and enter into a dialogue with its members, or had I at least received an updated draft with the new charges and grounds for such charges for me to comment upon. I had requested permission to appear before the DCSD, but was refused.

It is my opinion that this is not only a matter of importance to myself: it also has considerable secondary consequences for the conduct of research in Denmark. Thus, I have drafted this document with my comments on the decision dated 18 December 2013 for the purpose of informing those who may have an interest in the case.

In the following, I would like to point out four crucial points of criticism towards the DCSD's decision.

The four points of criticism towards the DCSD's decision

1. The DCSD are mistaken with respect to the years of the sequence of tests in three articles and thus make a serious factual error in respect of selection.

The DCSD have misunderstood the years of and sequence of the tests mentioned in Articles 6, 7 and 10. In Articles 6 and 7, from 2005 and 2006 respectively, seven test persons were included, who had muscle biopsies taken from their arm (*m. triceps brachii*), thigh (*m. quadriceps*) and lower leg (*m. soleus*). It was these muscle samples from the same seven persons that were used to test different hypotheses in the respective articles. There were 14 test persons in Article 10 from 2007: i.e. seven more test persons were added to the original seven. The DCSD accuse the authors of selecting from among the 14 test subjects from 2007 for the 2005 and 2006 articles. They thus, even in their own grounds for their decision, make the completely obvious mistake of turning the time axis 180 degrees and assume that, out of the 14 (in the 2007 population), seven were selected for the articles published in 2005 and 2006 – when it is exactly the opposite that is true: that an *additional 7* persons were included in the 2007 article.

In the draft decision of June 2013, the DCSD had argued that the 14 test subjects in Article 10 were different from the seven in Articles 6 and 7. I pointed out in my response to the draft decision that this was not the case. In his complaint, Galbo stated that the 14 test subjects were the seven 'old ones' plus seven new ones, which I did not dispute, since this was correct. It was certainly not a case of undisclosed selection of seven from a group of 14, but the opposite.

After announcing their final decision, the DCSD contacted the journals in which the articles in question had been published. One of the journals (JAP) contacted the group of authors and requested an explanation regarding Article 7. I am neither first nor last author, nor am I the corresponding author, but my colleagues – i.e. Peter Plomgaard, the first and corresponding author, and Henriette Pilegaard, the last author – has responded to the journal that the issue is based on an error on the part of the DCSD. As the DCSD erroneous decision has indirectly accused these authors of scientific dishonesty, they will continue to clear up the matter at their own expense.

Neither I, as the defendant, nor my co-authors have been heard on this charge, which was neither raised in the original complaint nor contained in the preliminary draft decision.

2. The DCSD drew an incorrect conclusion about selection in an article.

The fact that we in one study performed some tests on all the test subjects, while a single test was performed on fewer test persons (which was correctly stated in the article's figure legend), resulted in a ruling of misconduct for selection (Article 4). This is a completely erroneous conclusion.

The DCSD assume that reporting of the results from one test comprising 11 test persons (six that had engaged in physical exercise and five in a resting control group) in an article including 18 test persons (12 that had engaged in physical exercise and six resting) is a manifestation of selection based on undisclosed criteria. It is clear that research results can be manipulated by only including 'good' test subjects; however, this is not the case here. The circumstances were simply that the size of the biological samples (collected under difficult conditions) taken from the 18 subjects were not sufficient to permit all tests to be carried out on all the test persons, and with regard to one of the tests, it was only possible to perform the analysis on 11 subjects (distributed as mentioned above). It clearly appears from the article that the part of the study in question only included 11 of the total of 18 test persons.

The fact that, for logistical reasons, some of the tests could not be carried out on all the test subjects, occurs extremely commonly in human physiology studies, not least when the test material is difficult to obtain (e.g. biopsy material). It is the exception rather than the rule that one runs out of material at the same time for all the test subjects. The material obtained should be used to the greatest possible extent. In this specific case, we concentrated on obtaining muscle biopsies of a quality that permitted embedding for analysis of the immunohistochemical expression of protein. Not until subsequently did the desire arise to supplement this analysis by also measuring RNA expression. However, material for mRNA had not been prioritised and for this reason was only available for 11 of the 18 test persons. This appears from the article and, furthermore, was also specified in my response to the DCSD draft decision of June 2013.

Because – as clearly appears from the article – we endeavoured to recruit a homogeneous population of test subjects, there was no need to separately describe the 11 test subjects, because the characteristics of the group (age, sex, BMI and physical fitness level) were not different from those of the remaining seven of the 18 test subjects.

The DCSD wrote that this was a manifestation of a serious violation of good scientific practice similar to undisclosed selection or surreptitious discarding of undesired results. It is a completely erroneous representation of the actual circumstances. All the results were presented. There was neither a selection nor a discarding of results, and the scientific product is fully transparent to the reader.

It is unfortunate that the DCSD, in their English translation of the press release, made an erroneous, misleading and defamatory statement in writing the following about the decision: 'As the lead author of the article, the Defendant was involved in the decision only to take certain readings (results) from a selected part of the total test population.'

3. The DCSD make use of arguments from my own response regarding disagreement over the use of cross-references to sharpen their conclusion in the final decision to my now being wilfully dishonest in omitting cross-references, instead of concluding that there is apparently disagreement in the scientific community on what constitutes good scientific practice in the field and without presenting counter-arguments or counter-evidence with respect to 'the legal basis'. The decision is, to put it mildly, peculiar.

In the DCSD preliminary draft decision from June 2013, I am criticised for having used the same muscle biopsies for testing different hypotheses in different articles without providing cross-references. In my response, I drew attention to the fact that there are no legal requirements, executive orders or other legal material that state rules for publications that use the same biological material for testing several hypotheses without providing cross-references. There are no requirements included regarding cross-references or references in the one direction (from the later article to the earlier one) in the DCSD guidelines, not even in the latest version of the DCSD guidelines from 2009. Neither are there any requirements regarding cross-references in the authors' instructions from the relevant scientific journals. The DCSD do not actually take a position on this line of reasoning, but simply state that they have a different opinion of how the Vancouver rules should be interpreted.

When the DCSD preliminary draft decision was published in the press in June 2013, a discussion arose about the use of biological material and cross-references that prompted a statement and a signature petition from 70 researchers publicly criticising the DCSD's handling of the cross-references issue.

On page 4 of its 2003 report, the Danish Agency for Science, Technology and Innovation working group for a research code of conduct wrote the following:

Ideally, it should be absolutely clear to the individual researcher and to the research community as a whole what is meant by scientific misconduct, what specific circumstances could give rise to the institution of misconduct proceedings, and under what conditions a researcher could be found guilty of scientific misconduct.

There is a huge difference between what the DCSD state in their draft decision of June 2013 about what good scientific practice requires in regard to cross-references and what is now indicated in their final decision. In their draft decision, the DCSD argue that omission of a cross-reference can be of methodological importance in understanding how the material was stored, might be degraded, etc. In their final decision, the DCSD accept my review of and conclusion that there are no specific methodological problems in our articles being withheld from the reader by our not providing cross-references. Further, the DCSD complain in their draft decision that omission of cross-references can lead to mass significance, but also accept my repudiation of this complaint in their final decision. The DCSD are now, in their December 2013 decision, putting forward a completely new argument: that it cannot be ruled out that information of scientific significance is being withheld from the reader through the omission of cross-references.

The DCSD argue that readers can be misled to believe that the material was gathered independently and originally, but do not at all address my argumentation that this is irrelevant and that a "biobank-view" should be taken. In the studies mentioned, we included homogenous groups of healthy subjects who followed a strictly defined protocol. This type of extremely demanding and invasive experiments will typically be organised with a view to testing one, two or more specific hypotheses, each with its own endpoint. Later, new hypotheses emerge that permit the same material to be used for new purposes. Gradually, the biological material is used up, and new studies may be organised with the same protocol and inclusion criteria for test subjects with a view to obtaining an n-value sufficient for new studies. It is crucial to understand that, for our actual testing, we recruited groups of *homogeneous* test subjects. Thus we did not study the biological variance, but used test subjects in basic physiological studies, following the exact same traditions and methods as are used in conducting physiological studies on mice or rats, for example. In such animal studies it would not be stated either, if some of the biological material had been used in previous studies to test other hypotheses.

Biological material taken from human test subjects, often under conditions that are stressful to them, must be used, right down to the last muscle fibre or drop of blood, to shed light on relevant scientific problems. Anything else would be unethical. Test subjects, test design and the biological material must, of course, be presented clearly in the scientific publications, in which the research results are published. From a scientific point of view, on the other hand, it is not necessarily relevant whether samples from the same biological material taken under the same test conditions were used or would be used for other scientific purposes. However, one might wish to shorten the description of the methods used, for example, and for this reason use a cross-reference to refer to a previous study.

In my opinion, it is clear that, in research circles, there is a great deal of disagreement about or very little support for the DCSD's view of cross-references. But rather than ruling in my favour or at least giving me the benefit of the doubt, it is surprising to see the DCSD instead hardening their stance in their final decision, now concluding that it is a matter of wilful misconduct because I argued that there are no legal requirements or executive orders that mention cross-references in connection with using material from the

same test subjects to test new hypotheses. Thus the DCSD write that “[the Defendant] has acted wilfully, as she stated that she is of the opinion that explicitly providing such information in an article is not required. Thus the Committee bases its decision on the fact that the Defendant deliberately refrained from providing information on the origins of the test material.”

Because I refer to the fact that the origins of the test material are reported in every single article, the DCSD’s conclusion is obviously incorrect: at the time the articles were written, it was definitely not set out anywhere that stating cross-references was obligatory, nor was it common practice. It is easy enough to insert a cross-reference in an article (provided that other studies in which the material is used have been published), but it did not happen in the cases at hand because it was not common practice, nor was it prescribed anywhere. Going forward, one might, of course, imagine guidelines being drafted on a line with the DCSD’s view of when cross-references are required and when they are not, to the effect that they would be required if studies were performed in the same subject area, but not required for non-related subjects. It would be natural for this to become part of the discussion going forward, i.e. the discussion on good research practice in Denmark that is being initiated at the ministerial level. However, as is exemplified below, it is difficult to clearly define when scientific subjects/topics are related and when they are not – and, in any case, it is an expression of a peculiar kind of logic when the DCSD use my own arguments against me in the matter of cross-references, given the lack of a clear-cut ‘legal’ basis. Instead of finding that the disagreement over the use of cross-references is evidently so great that one cannot reach a conclusion with any certainty, the DCSD elect to sharpen their opinion in the final decision by ruling that I am guilty of wilful misconduct – this in spite of the fact that a great many reputable researchers here in Denmark share my view of the correct use of cross-references.

4. The DCSD introduce entirely new boundaries for when the omission of cross-references should be considered misconduct. These boundaries lack legal basis and must be considered highly dubious.

In my response, I explained how my group’s cross-referencing practices were, at the time of publication, in accordance with standard practice. I pointed out, substantiated and documented my statement by presenting documentation of the fact that many researchers – also the DCSD Committee’s own members and professor Galbo who lodged the complaint against me – have to a great extent used the same biological material in several articles without providing cross-references in the methods section, but occasionally have done so in the introduction and/or discussion section (please see the tables in my response).

In contrast to their position in the preliminary draft decision, the DCSD now conclude in their final decision that it is not *always* directly dishonest to omit cross-references, but the DCSD deem it true of a number of my articles that the omission of cross-references in the methods section while providing these references in the discussion is misconduct. The Committee maintains that, in the case of some articles, cross-references must be provided when it is a matter of the same scientific subject areas within health sciences and concludes that, in articles about protein expression in human muscle as a response to exercise, it is scientifically dishonest to omit cross-references (Articles 1, 3, 4 and 5), whereas in Articles 6, 7 and 10, which are about protein and mRNA expression in different muscle groups, it is not dishonest to omit cross-references. According to the DCSD, in some cases (Articles 1, 3, 4 and 5), it constitutes aggravating circumstances that the same group of authors is involved, but this argument is not made in other cases (Articles 6, 7 and 10). If a cross-reference is stated in the discussion but not in the methods section, it is misconduct, according to the DCSD: a practice that is otherwise common, as documented in the previously submitted material (please see the tables in my response).

This differentiation between when the omission of cross-references is scientific dishonest and when it simply falls under the category of ‘not good scientific practice’ is certainly not rooted in any kind of reflection or deliberation and is the first of its kind to be seen. The lack of transparency in the

determination of what is misconduct and what is not misconduct is in direct contravention of what the Danish Agency for Science, Technology and Innovation working group wrote on page 4 of its 2003 report:

The procedure followed in the consideration of a case should be as transparent as possible and subject to the highest possible level of due process protection for the researcher against whom a complaint has been filed.

With the DCSD's decision, it will be very difficult for Danish researchers to determine in which cases they could retrospectively risk a verdict of misconduct for having omitted cross-references, as not even the DCSD are consistent in the rules they put forward on this occasion, rules which were not stated in connection with the draft decision and thus had not been submitted for the consideration and response of interested parties.

Regarding other misconduct findings in the DCSD final decision

In contrast with their preliminary draft decision, the DCSD in their final decision in seven instances withdraw their claim of my being co-responsible for Milena Penkowa's image manipulations, but maintain that I should have discovered the manipulation in one instance. The DCSD thus declare that I was dishonest in connection with a publication that I requested be withdrawn in 2011 when I discovered that Penkowa had cheated. The accusation of gross negligence in this specific case is based entirely on an assessment by the DCSD.

In addition, the DCSD are dropping the misconduct charge included in the preliminary draft decision in connection with two articles, acknowledging now that it was actually technical errors. However, the DCSD do uphold one accusation of gross negligence in connection with an erroneous description of a group of test subjects. A section had been deleted by mistake at some point in the editing process, so by 2011 we had already submitted an erratum that was accepted by the journal. I agree with the DCSD that the erratum should have emphasised the fact that some of the test subjects had completed a two-hour and others a three-hour bicycle exercise session, but in my opinion this is a detail in the design of the experiment that was not crucial to the scientific conclusions of the article.

Conclusion

It offends me that I can be declared guilty of scientific dishonesty when I have not cheated.

The DCSD is committing a grave formal error by producing new complaints and arguments that were neither included in the complaint itself nor mentioned in the draft decision and thus not submitted for the consideration of and response from interested parties. The DCSD are also making a grave factual error regarding selection, advancing accusations of misconduct without the authority to do so under current rules, regulations or law. Overall, there are so many grave errors in the DCSD's final decision in my case that it should have consequences.

All the same, I sincerely regret any damage that the matter may have caused, and I will do what I can to ensure that it will have the least possible consequences for Rigshospitalet - Copenhagen University Hospital, the University of Copenhagen, my research group and the foundations that support our research.



Bente Klarlund Pedersen