Vaccination against the swine flu in 2009

In issue no. 7/2012 of this journal, Director Geir Stene-Larsen of the National Institute of Public Health claims that the swine-flu vaccine Pandemrix had been clinically tested and that my assertion in an editorial in issue 5/2012 that it had not been clinically tested therefore is wrong (1, 2).

I should of course have used different wording, since «not clinically tested» is a very imprecise expression. Instead, I should have written «insufficiently clinically tested». In particular, insufficiently clinically tested to recommend vaccination of the entire Norwegian population. That was my point.

Clinical tests of a drug can be very diverse: From the very earliest stages, with small trials on humans – often performed by the manufacturer of the drug – to see whether the drug is harmful, i.e. has frequent and serious side effects (phase 1 studies) to comprehensive studies that balance the drug’s effects against side effects that can be of a serious as well as a less serious nature (phase 3 studies). Solid phase 3 studies are commonly required before a drug can be approved by the authorities. Since these studies also may fail to detect rare, but serious side effects, the authorities increasingly often require systematic follow-up studies (phase 4 studies). In other words, more than ordinary reporting of side effects.

How the potential effect of a drug can be balanced against potential side effects depends on the group of patients that will use the drug. For seriously ill patients who have few other treatment alternatives, even quite serious side effects may be deemed acceptable if an effect is possible. For healthy people facing a disease which is harmless to the vast majority, there must be four protein bands in the CERA position and free of error (2). This is a remarkable statement, in light of the fact that 94 independent experts, including 45 professors, have signed a declaration saying that data produced by the WADA laboratory in Rome fail to detect CERA in Tysse’s urine. See also a reply by Waaler and collaborators (3). Of the two methods used, the isoelectrophoresis (IEF) method has yielded results of a very poor quality, which makes it hard to interpret the data. WADA has attempted to improve them by manipulating the raw data with the aid of cut-and-paste techniques, as demonstrated during the proceedings of the Court of Arbitration for Sports (CAS) in Lausanne.

The background for the manipulation is that the technical document published by WADA requires four protein bands that must correspond to bands in CERA reference protein. This criterion was clearly not fulfilled. During the CAS hearings, the technical requirement for four corresponding bands was changed to saying that there must be four protein bands in the CERA area in the IEF analyses. The legal experts on the arbitration panel accepted this change, which significantly weakens the requirements for a positive test. If the analysis results produced by the IEF method are uncertain, SDS-PAGE analyses can be used. In Tysse’s case, this analysis shows that none of the proteins correspond to CERA reference protein. A very weak protein band that moves further than CERA was claimed by WADA as evidence of this. However, this weak protein band was also detected in control urine, which shows conclusively that Tysse’s urine does not contain CERA. WADA chose to ignore this analysis, and this was condoned by the CAS arbitrators. Professor Werner Franke, who is an outstanding researcher in the field of cell biology and well known for having exposed the systematic doping that took place in the former East Germany, testified in the case by telephone. He concluded that SDS-PAGE is a more reliable analysis method than isoelectrophoresis for separation of such molecules, and that the absence of protein bands in the CERA position shown by SDS-PAGE is proof that there is no CERA in the sample. In the reasons for the judgement this was misconstrued to say that Franke was of the opinion that «SDS-PAGE analysis is completely unreliable and cannot be used to convict or to sentence an athlete for doping».

WADA has refused to undertake alternative analyses of the urine sample or to allow analyses to be performed in another laboratory accredited by WADA. This is one of several examples showing that WADA is not interested in putting scientific facts at the forefront in this matter. For those who are interested in reading a more exhaustive discussion of these analyses we recommend our two opeds in Bergens Tidende, written after the case had been processed in Oslo (4) and Lausanne (5) respectively. We were the only Norwegian experts who attended the processes in both locations. We wish to emphasise that we have received no financial remuneration for our involvement in this matter.

Bjarne Østerud
Tromsø

Tore Skotland
Oslo

Bjarne Østerud (born 1940) is Professor of Biochemistry at the Faculty of Health Sciences, University of Tromsø. His specialty is haemostasis and thrombosis, and he is a board member of the International Society on Thrombosis and Haemostasis (ISTH). Conflicts of interest: The author has acted as advisor to Tysse in this matter, but has received no financial compensation for this.

Tore Skotland (born 1947) is a biochemist and dr.philos. For many years he directed the work on bioanalysis of all contrast agents developed by Nycomed/Amersham/GE Healthcare, and is currently Guest Scientist at the Centre for Cancer Biomedicine at Oslo University Hospital, Radiumhospitalet.

Conflicts of interest: The author has acted as advisor to Tysse in this matter, but has received no financial compensation for this.

References

Doping analyses are not on safe ground

In their comments on the so-called Tysse affair (1), Hemmersbach and collaborators claim that doping analyses are on safe ground and free of error (2). This is a remarkable statement, in light of the fact that 94 independent experts, including 45 professors, have signed a declaration saying that data produced by the WADA laboratory in Rome fail to detect CERA in Tysse’s urine. See also a reply by Waaler and collaborators (3). Of the two methods used, the isoelectrophoresis (IEF) method has yielded results of a very poor quality, which makes it hard to interpret the data. WADA has attempted to improve them by manipulating the raw data with the aid of cut-and-paste techniques, as demonstrated during the proceedings of the Court of Arbitration for Sports (CAS) in Lausanne. The background for the manipulation is that the technical document published by WADA requires four protein bands that must correspond to bands in CERA reference protein. This criterion was clearly not fulfilled. During the CAS hearings, the technical requirement for four corresponding bands was changed to saying that there must be four protein bands in the CERA area in the IEF analyses. The legal experts on the arbitration panel accepted this change, which significantly weakens the requirements for a positive test. If the analysis results produced by the IEF method are uncertain, SDS-PAGE analyses can be used. In Tysse’s case, this analysis shows that none of the proteins correspond to CERA reference protein. A very weak protein band that moves further than CERA was claimed by WADA as evidence of this. However, this weak protein band was also detected in control urine, which shows conclusively that Tysse’s urine does not contain CERA. WADA chose to ignore this analysis, and this was condoned by the CAS arbitrators. Professor Werner Franke, who is an outstanding researcher in the field of cell biology and well known for having exposed the systematic doping that took place in the former East Germany, testified in the case by telephone. He concluded that SDS-PAGE is a more reliable analysis method than isoelectrophoresis for separation of such molecules, and that the absence of protein bands in the CERA position shown by SDS-PAGE is proof that there is no CERA in the sample. In the reasons for the judgement this was misconstrued to say that Franke was of the opinion that «SDS-PAGE analysis is completely unreliable and cannot be used to convict or to sentence an athlete for doping».

WADA has refused to undertake alternative analyses of the urine sample or to allow analyses to be performed in another laboratory accredited by WADA. This is one of several examples showing that WADA is not interested in putting scientific facts at the forefront in this matter. For those who are interested in reading a more exhaustive discussion of these analyses we recommend our two opeds in Bergens Tidende, written after the case had been processed in Oslo (4) and Lausanne (5) respectively. We were the only Norwegian experts who attended the processes in both locations. We wish to emphasise that we have received no financial remuneration for our involvement in this matter.

Bjarne Østerud
Tromsø

Tore Skotland
Oslo

Bjarne Østerud (born 1940) is Professor of Biochemistry at the Faculty of Health Sciences, University of Tromsø. His specialty is haemostasis and thrombosis, and he is a board member of the International Society on Thrombosis and Haemostasis (ISTH).

Conflicts of interest: The author has acted as advisor to Tysse in this matter, but has received no financial compensation for this.

Tore Skotland (born 1947) is a biochemist and dr.philos. For many years he directed the work on bioanalysis of all contrast agents developed by Nycomed/Amersham/GE Healthcare, and is currently Guest Scientist at the Centre for Cancer Biomedicine at Oslo University Hospital, Radiumhospitalet.

Conflicts of interest: The author has acted as advisor to Tysse in this matter, but has received no financial compensation for this.