

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 a healthy population facing a disease which is harmless to the vast majority, there must be extremely good documentation of effects in order to allow any side effects – frequent or rare – whatsoever.

Stene-Larsen and the Institute of Public Health claim that the vaccine had been clinically tested to a «sufficient» extent, even though the tests had been performed on a similar vaccine against another virus, the bird-flu virus H5N1. However, the response to the virus itself is the decisive factor for effects as well as side effects, so the studies of the bird-flu vaccine had a limited transferability to the swine flu.

Stene-Larsen further says that the Institute of Public Health delayed the decision to recommend the swine-flu vaccine to everybody until 23 October 2009, since «on that date we had evidence that Pandemrix did not produce frequent, serious side effects». This logic is flawed. When recommending a vaccine to an entire, healthy population and knowing that the disease is harmless for the vast majority, it is insufficient to ensure that the vaccine does not pro-

duce «frequent, serious side effects». It must also be ascertained that it is effective to an extent that offsets the risk of the very rare, but serious side effects that tend to occur – unfortunately also in this case.

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References

1. Stene-Larsen G. Vaksinasjon mot pandemisk influensa 2009. Tidsskr Nor Legeforen 2012; 132: 786–7.
 2. Haug C. Hva visste de, og når visste de det? Tidsskr Nor Legeforen 2012; 132: 505.
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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.

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

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