Bioteknologinemnda
The Norwegian Biotechnology Advisory Board

Det Kongelige Helse- og omsorgsdepartement
Postboks 8011 Dep
0030 Oslo

Vår ref: Deres ref: Dato: 1/9-2006

Høring: OECD – Foreslåtte retningslinjer for kvalitetssikring av molekylær-genetisk testing

Vi viser til brev av 28 juli 2006 med oversending av ovennevnte for kommentarer. Bioteknologinemnda skal ha sitt første møte etter sommerferien den 31. august. Høringsfristen er satt til 28. august for innspill til Helse- og omsorgsdepartementet for oversendelse til Nærings- og handelsdepartementet, men vi har fått utsatt høringsfrist til etter nemndsmøtet den 31. august.

Bioteknologinemnda har i sitt høringssvar vektlagt å komme med forslag til hvor det bør arbeides videre med å utvikle retningslinjene innenfor vanskelige områder i den kliniske hverdag. Disse er presentert under.

Denne høringsuttalsen har 2 deler:
1. Mer overordnede kommentarer som er av nasjonal betydning
2. Momenter som kan oversendes til OECD og derfor utarbeidet på engelsk

Bioteknologinemnda vil legge ut høringssvaret på vår hjemmeside på vanlig måte, og vi gir derfor OECD tillatelse til å offentliggjøre vår uttalelse med vårt navn.

Vi ønsker i denne sammenhengen først å informere HOD og NHD om at Bioteknologinemnda har ved flere anledninger arbeidet med gentester. Vi vil her fremheve at det ble avholdt et fagseminar om regulering av gentester i klinikk den 7. juni 2006 sammen med Sosial- og helsedirektoratet. Her deltok representanter for alle de medisinsk-genetiske fagmiljøer i landet for å drøfte hva og hvordan dette fagfeltet burde reguleres. I denne forbindelse ble internasjonale initiativer fra OECD og Europarådet presentert. En rapport som innholder de fleste innleggene på møtet finnes på www.bion.no/publikasjoner.shtml. I tillegg vil vi nevne at vi har utarbeidet et temaark om gentester (www.bion.no/skole). Temaarket er ett av en samling slike som skal inngå i

en informasjonspakke; ”Moderne bioteknologi”. Informasjonspakken utarbeides spesielt med henblikk på skolen. Temaarket om gentesting var også med som et utrivingsbilag til GENialt (nr. 2, 2006) som distribueres gratis til over 8000 abonnenter.

Bioteknologinemnda ønsker å berømme arbeidet i OECD-arbeidsgruppen for initiativet og grundigheten i arbeidet, og anbefaler at det blir lagt til grunn for det vider arbeidet med kvalitetssikring av gentester i Norge. Molekylære gentester ser ut til å bli brukt stadig mer, og det er et økende kommersielt marked. Siden resultatene fra slike gentester kan ha stor medisinsk betydning for andre enn den det gjelder i forbindelse med diagnostisering og behandling av sykdom, kan feil resultater fra gentester få vidtrekkende konsekvenser også for andre familiemedlemmer.

Bioteknologinemnda gir sine kommentarer tematisk med henvisninger til nummereringene i dokumentet siden temaene er berørt på flere steder i dokumentet.

Vi ønsker å påpeke at dersom man går til det skritt å akkreditere de laboratorier som skal utføre gentester ved hjelp av utenforstående tredjepart, vil dette kunne få økonomiske konsekvenser (betale akkrediteringsinstitusjon og tid for dokumentasjon og deltagelse i prosessen). Akkreditering behøver ikke bli dyrere enn andre prosesser for dokumentasjon av kvalitet i laboratoriearbeidet. Kostnaden vil varie veldig med hva som akkrediteres. Nemnda ønsker ikke å gå inn i spørsmålet om forskjellige måter for akkreditering eller autorisasjon, men nøyer seg med å påpeke at akkretditering eller autorisasjoner er den mest effektive måten å minke markedet for useriøse aktører dersom man samtidig offentliggjør hvilke offentlige og private aktører er det som er kvalitetssikret. HOD bør derfor spesifisere hvordan eventuelle endringer i prosedyrer for autorisasjon/akkreditering skal gjennomføres (administrativt og økonomisk).

Bioteknologinemnda mener at det i det videre arbeidet med gentesting i Norge, blir viktig med et tett samarbeid mellom SHdir, Bioteknologinemnda og de nyetablerte norske nettverket for medisinsk genetikk. Nettverket vil være spesielt verdifullt med hensyn på hvorledes gentesting i Norge kan reguleres på en hensiktsmessig måte.

Bioteknologinemndas høringssvar til OECD

Comments from the Norwegian Biotechnology Advisory Board

Quality assurance of the laboratories
The guidelines are developed for use within medical healthcare in general **(preface, scope and A2)**. This means that molecular genetic test providers should be treated in an equal way as far as they are providing genetic tests, whether they are commercial or not **(part II, 25 A8)**. It should furthermore be stressed that both molecular genetic tests and cytogenetic tests are included.

Genetic testing in forensic medicine is not within the scope of these guidelines. The Norwegian Biotechnology Advisory Board regards these guidelines as highly relevant also in forensic medicine and would like to recommend that The Ministry of Justice and police is informed about

these OECD guidelines. The consequences of poor quality of molecular genetic testing can be critical also for individuals in forensic medicine. We are aware of that many forensic laboratories are working with different systems for either accreditation or certification. Since OECD has a large influence, The Norwegian Biotechnology Advisory Board suggests that guidelines should also be used in this field, which could be helpful for those countries that have not started on such processes.

The need for quality assurance systems is obvious for genetic tests used in diagnostics. The Norwegian Biotechnology Advisory Board supports the OECD guidelines for the quality control of the laboratories, and is pleased that the guidelines not only cover the analytical work, but also information to the patients and health workers, and training of staff. The guidelines point out the importance of transparency and ethics in genetic testing. According to Norwegian Act of application of biotechnology in human medicine (§ 7-1) labs providing genetic testing must have authorisation.

The Norwegian Biotechnology Advisory Board suggests that the OECD guidelines should be followed regarding authorisation of the unit which is proving molecular genetic tests. The Norwegian Biotechnology Advisory Board regards that it is important that the guidelines cover the complete process of genetic testing as outlined.

Validity and use of molecular genetic tests

One critical part of molecular genetic testing is the validity and relevance of the results for its application in a clinical situation, and with particular respect to the population served by the laboratories (**Bv** and mentioned in section about information to patients **Dvii)**. The Norwegian Biotechnology Advisory Board is therefore pleased that the guidelines specify that the interpretation of the results given in the report should contain:

> "An interpretation of the genotype in the context of the indication for testing and other relevant demographic (*i.e.* race, ethnicity), clinical and family-specific information, including clinical sensitivity and specificity. The interpretation should be developed to ensure that the recipient of the report is able to understand the clinical usefulness and limitations of the test result". **(Dvii)**

This is a challenge to the health systems since there can be conflicts of interest between the provider of genetic tests, the patients, and the institutions that are paying for the service. Irrelevant genetic tests, or tests where links between genetic variants and clinical manifestation is not clear, can give extra burden to the patient and costs to the health system, but more money for the institution proving the tests. The guidelines do not provide any information about how to solve this problem about the relevance of the tests, although this problem has been addressed by the molecular genetic testing institutions themselves.

The Norwegian Biotechnology Advisory Board suggest that Norway should encourage OECD to elaborate on this difficult topic and hopefully suggest guidelines for how to ensure validation of the tests to ensure that only the clinical relevant tests are used in clinical practices.

The Norwegian Biotechnology Advisory Board also suggest that The Directorate for Health and Social Affairs (SHdir) and The Norwegian Biotechnology Advisory Board collaborate with and stimulate the newly established Norwegian network for medical genetics in evaluation of relevant molecular genetic test for the different clinical conditions. **(Part II, 27 and 28 (Aii, Aiii))**

Competent authority
The Norwegian Biotechnology Advisory Board notices the focus on the importance of a competent authority to ensure proper regulation and incentives for the labs. The authority shall also establish certifications (by third parties) and professional feedback on control routines and annual reports **(B5, B7)**. Dialogues between the authority and labs are important parts of quality control in genetic testing **(section C** and in "best practices" **Ci to Cvii)**. A system for management of these processes has to be in place to retain the confidence of the public.

Information to the patients
The Norwegian Biotechnology Advisory Board acknowledges the detailed description of relevant information presented to patients undergoing genetic testing **(Aii)**. To have such a list to follow **(section D, Dvii)** not only improves the quality of the information to be given, but also the efficiency in the work to be done when providing the written report on the tests to the health workers **and** to the patients. It is noteworthy that the information is both detailed and technical. This gives the knowledgeable/informed patient a possibility to participate in the process concerning own health and quality assurance of the processes **(part II, 59. (Di, Dii))**. The labs should provide information (analytical, clinical validity and utility) also before the genetic testing to ensure that the consent is informed.

Education and training of staff
The guidelines include training and education of staff and management of molecular genetic test laboratories **(section E and 72. (Eii))**.

The Norwegian Biotechnology Advisory Board is pleased that multidisciplinarity is addressed in details. The guidelines should therefore be communicated to hospitals and universities with such units by the competent authority to ensure training and educational qualification of the staff and the leaders, and to ensure that the most competent people are employed, and balanced teams are built.

Genetic testing in a network
There are international networks for rare disorders, with collaboration regarding reference families and clinical material and exchange of knowledge and results. Such systems are of great benefit for the patients, but not necessarily to the molecular labs themselves. This may be a challenge for the health care authority. The competent national authority has to be brave enough to promote economical incentives for collaborations instead of developing test facilities many places in Norway for rare disorders.

The Norwegian Biotechnology Advisory Board is aware that there is an initiative among the molecular genetic labs in Norway to specialize and take responsibility for the different genetic tests provided by the authorized labs. In this way the labs themselves have initiated processes to provide better service to the patients and more economical for the authorities **(part II, 46. (C5, Cvi))**.

Research and clinical use
Many institutions are running analytical clinical services **and** researching genetic disorders on the same patients. New knowledge means new genetic tests. Many molecular genetic test are therefore performed in a research context and the validity of the genetic test is therefore not known **(part II, 54. (D1))**. The guidelines address this issue. The Norwegian Biotechnology

Advisory Board suggests that this challenge should be addressed in more detail by OECD, and suggests that OECD continues the work and that attempts should be made to provide guidelines to this problem. It is of importance to be able to draw some kind of line between what is research and what is to be used in a clinical setting and become a part of the patient's journal.

Yours sincerely

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Chairman

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Director