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Dear Mark

Re. Human Genetics Commission's advice on free fetal DNA testing

In response to your letter of 17th December, the HGC agreed to gather information and provide advice about likely concerns relating to the introduction of free fetal DNA testing into clinical practice. Accordingly, we arranged a session at our recent plenary meeting in Cambridge involving three speakers (Dr Lyn Chitty, Consultant and Reader in Genetics and Fetal Medicine, Institute of Child Health, Dr Helen White, Senior Scientist, National Genetics Reference Laboratory, Wessex, and Professor Martin Bobrow, Professor of Medical Genetics at Addenbrooke's Hospital, Cambridge) and an invited audience. (The audience included a number of representatives from the PHG Foundation, which has a project underway – due to report in Autumn 2008 -- to develop a strategy for the implementation of the technique for different health service applications and we heard from Dr Hilary Burton of the Foundation in relation to this.)

Summaries of the presentations and full minutes of the discussion will shortly be available on the HGC website but I write now to confirm the points on which the Commission were agreed following the meeting. I shall

respond, under separate cover, to the other issue raised in your letter in due course.

You will recall that the session on free fetal DNA was both lively and informative, and the discussion, first within the Commission and then involving the audience, revealed a range of opinion about the appropriate conditions under which the technique should be introduced as a clinical service.

In summary, the Commission's advice is as follows:

- We find the technique to offer a promising diagnostic strategy for some specific conditions. We recognise the great value to patients of having both an early diagnosis (at around seven weeks' gestation), and one which is non-invasive and presents very little risk to mother or fetus compared with currently available alternatives. We also recognise the considerable technical challenges in developing the technique for new applications such as testing for chromosome abnormalities.
- However, we do not feel that free fetal DNA analysis has been sufficiently thoroughly evaluated as a test (rather than as an assay), i.e. for the specific purposes for which it is to be used, and we therefore find its introduction as a clinical service in some centres to be premature. In particular, the Commission is concerned that where the technique has found support among clinical professionals it appears to have entered the NHS as a service, with the implication that Trusts which refer patients for testing will receive a bill for a service which has not yet been properly evaluated.
- We agree with Professor Bobrow's proposal that independent evaluation of the technique should be carried out within the scope of a multi-centre research project with research ethics committee approval, in order to allow standardisation of conditions and parameters, such as indications, patient information and clinical pathways.
- The observation relating to the way in which this technique has been taken up has highlighted an inconsistency of approach to the introduction of new diagnostic techniques. A well-developed pathway exists, via the UK Genetic Testing Network's Gene Dossier submission process for tests for new genetic variations, but that route has not been followed in relation to free fetal DNA testing (which is essentially a new technique to test for established variations). We feel that similar concerns could arise in future with established assays being used for new purposes or entirely new techniques being applied for variations for which there is already an established test. As a minimum, we feel that

there is a need for a clear and consistent distinction between when a test is being used within a research study or as part of an established service. This would bring clarity for patients and support the better development of services as well as providing a useful indication to service commissioners and research funders about appropriate allocation of resources.

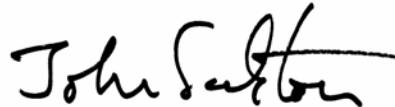
- It is recognised that there is a lack of readily identifiable sources of funds for what has been described as phase 2 translation in diagnostics, analogous to phase three clinical trials. This is a matter which would benefit from further discussion with relevant parties.
- More broadly still, we recognise the potential for the technique to be offered outside an NHS setting, for example by commercial providers or over the internet, and we would re-emphasise the points made in our recent report *More Genes Direct* with respect to direct-to-public marketing. In particular, the capacity of this technique to identify fetal sex, raises concerns that it will be used for the purpose of sex selection for non-medical reasons. Its potential to resolve uncertain paternity may also constitute cause for concern where obtaining consent to the analysis of samples from a putative father is not carefully overseen.

I will be writing separately to Professor Sally Davies, Director-General of Research and Development at the Department of Health, to indicate to her that we feel further evaluation of this technique is a matter of priority.

I would welcome your thoughts on how the HGC can further assist the government in relation to antenatal screening and on broader issues within our remit.

As before, I am copying this to Gareth Jones, Anthony Whitehead (DIUS), Ros Skinner (Scotland), Rachel Brown (Wales) and David Galloway (NI).

Yours sincerely,

A handwritten signature in black ink, appearing to read 'John Sulston', with a stylized, cursive script.

John Sulston
Acting Chair, Human Genetics Commission