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Dear Dr Lee

Thank you for your letters of 7 April and 17 May about recombinant Factor VIII. I read your letter to the Lancet with interest.

I would offer first some general comments and, then, some observations on hepatitis A and parvovirus mentioned in your letter to the Lancet.

As you are aware, it is generally accepted that the treatment of patients with blood and medicinal products derived from human blood and plasma is not without risk. Safeguards have been put in place to minimise the risk of transmission of viruses. The safety of blood products depends on a number of factors, which, taken together, reduce, as far as is possible, the risk of viral transmission. These include the screening of donors, the testing of donations, plasma pool testing and the ability of the manufacturing processes to remove or inactivate viruses, and viral marker tests that can be undertaken on certain finished products. They relate to the manufacture of all blood products, Factor VIII, immunoglobulins and albumin. Although steps are taken and will continue to be taken to minimise risk, these safeguards cannot guarantee, absolutely, the removal of that risk. Consequently, the treatment of patients with recombinant Factor VIII, containing human serum albumin as a stabiliser, is also not without risk.

Your statement about the hepatitis A problem needs to be put in context. As far as this is concerned, you will be aware that there is still not a universally accepted explanation of the cause of hepatitis A transmission with some batches of Factor VIII associated with one particular manufacturer. It appears that using identical methods of manufacture used by one Company and its licences, transmission occurred in product from some plants, but, not in others.

The evaluation of data submitted by manufacturers are kept under review by the CPMP and, also, by the MCA for products granted Marketing Authorisations. The CPMP has advised

that all blood products should have a validated step in the manufacturing process to remove/inactivate enveloped and non-enveloped viruses. This additional viral removal/inactivation step is aimed at the prevention of transmission of non-enveloped viruses, including hepatitis A.

It is however accepted that guaranteed freedom from possibility of parvovirus transmission will be extremely difficult. Parvovirus is an extremely common infection which may be asymptomatic or mild in many individuals. Most adults and children will come into contact with parvovirus through routes of exposure other than blood products. A high proportion of children and even more adults are immune. As you say, its effects may be more severe in patients with immuno-deficiency, chronic haemolytic anaemia or in fetuses. The relevance of this as a problem again needs to be considered in relationship to the population at large, many of whom have already been infected.

Taking into account the state-of-art regarding the manufacture and control of medicinal products derived from blood and plasma, some patients with haemophilia may benefit from treatment with recombinant Factor VIII. In your letter you refer to certain categories of patients where you would think recombinant Factor VIII may be appropriate. If this is the case, then you should be able to support this position on the basis of scientific and clinical need. I think you will agree, it is preferable to consider the individual circumstances of each patient with haemophilia rather than making generalisations.

I note in particular that you had identified children under the age of 10, where I presume the significance is that these are children who have not been infected with HIV and hepatitis C. Purchasers will, I am sure, seek assurance that the money they spend is determined by efficacy of treatment as well as value for money and related of course to individual patient circumstances.

Yours sincerely

GRO-C

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