



NATIONAL BIOLOGICAL
STANDARDS BOARD

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Dr. M.E. Duncan
Medicines Division
DHSS--
Market Towers
1 Nine Elms Lane
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Dear Mary,

Heat-Treated Factor VIII

Thank you for your letter of January 16th, accompanying the copy of the abridged application for a heat-treated product from Alpha Therapeutics. I think the submission indicates that the company has made a serious attempt to reduce the infectivity of their product. As you noted in your letter, they have used four marker viruses, including HTLV III, and have shown that their heat-treatment step inactivates at least down to the current level of detection of this virus. I cannot see what else we can expect them to do. Their treatment of Factor VIII is of course different from that of the other manufacturers and, as far as I know, they are the only one that is treating the material with heptane, followed by heating.

As you know, the main worry about these heat-treated products is whether evidence will emerge from long-term studies of the formation of neo-antigens and, particularly, antibodies to Factor VIII. I think the immunologists might claim that, on theoretical grounds, one might expect evidence of neo-antigens to develop eventually. All one can say, however, is that nobody has yet demonstrated their presence and that, in some 18 months of use in other countries, the problem does not seem to have developed in patients. I suppose it is reasonable to swap an uncertain hazard of antibody development some time in the future, for a very definite hazard from unheated Factor VIII in the present.

On balance, I think Alpha Therapeutics have made a reasonable case for their modified product. Once again, one is struck by the contrast between this submission and one or two others that you have sent to me.

DT5ACZ

I think the idea of a scientific meeting between NIBSC and manufacturers has merit, although I cannot see it taking place before late spring, at the earliest, due to other commitments. However, I will keep in touch with you if we do decide to go ahead.

With all best wishes,

Yours sincerely,

GRO-C

~~Duncan P. Thomas~~

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