NATIONAL BOARD OF HEALTH

Medicines Division

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Our ref. ES/bt

Your ref.

SUBJECT: PARALLEL IMPORT OF SANDOGLOBULIN, HUMAN NORMAL IMMUNOGLOBULIN FOR INTRAVENOUS ADMINISTRATION

Dear John,

As I briefly mentioned for you at our last Biotech meeting the quality of Sandoglobulin produced by Swiss Red Cross for Sandoz AG is perhaps not the same for the UK imported and Danish imported product. I should very much like to have it clarified as we can not have two different qualities of the same product on the Danish market.

Sandoz A/S (Denmark) got an marketing authorization for Sandoglobulin in Denmark 1984 and the file has been updated frequently since that. In 1991 we got an application from a parallel importer, who wanted to import Sandoglobulin from UK. We had correspondence with MCA to ensure that the two products were identical and that some of the most important key issues were fulfilled and the same.

- The production to ensure that the virus inactivation procedure was the same.
- The origin of the source plasma including donor centres and that every single plasma portion used for Sandoglobulin is tested and found negative for HIV-antibody and HBsAg.
- Control tests on the finished product.

MCA has been so kind to send all these informations with letter dated 15 November 1991 (copy enclosed). As these were identical with the imformations we had in the Danish file (apart from IgA test on the final product) I assumed that the UK imported and Danish imported product were the same including the quality and the marketing authorization was granted.

We have however now received a complaint from Sandoz A/S (Denmark). They claim that the quality of the two products are not the same. According to Sandoz A/S Denmark has some special demands to Sandoglobulin which require selection of special lots for the Danish market.

Address	*Telephone*	*Direct dial*	*Telex*	*Facsimile*
378, Frederiksundsvej DK-2700 Brønshøj Denmark	(10 a.m. to 3 p.m.) + 45 4494 3677	+ 45 4494 7077 + ext.	35 333 ipharm dk	+ 45 4284 7077

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The extra demands from the Danish authorities should be the following:

1. Microbiological in-process control.

   We have set an alert limits for the TVC in the plasma pool and on different essential production steps. The limits are 10^2 TVC per ml. Our philosophy is that the assurance of sterility should be obtained by avoiding microorganisms under the production and not only removing them .

2. Reprocessing of non sterile and pyrogenic products is not allowed.

   In the application for marketing authorization the company mentioned that reprocessing were done when the product were pyrogenic or non sterile. We asked for further information on which conditions this were done including stability considerations as the product in some cases were heated to 45°C for 73 hours. The responds from the company were not satisfactory and they promised then not to reprocess to the Danish market.

3. A limit for the max amount of IgA in the finished product

   The limit is 2 g IgA per litre 6% solution. The IgA content should be as low as possible to avoid anaphylactic reactions among patients with IgA antibodies.

I should very much like to know which requirements you have to the above 3 points. If you have no specific but only generel requirements I would ask you to comment on our demands and would very much like to have your opinion whether you would demand the same requirements in the future. It could be an issue for the Biotech group to discuss if we do not have the same opinions.

I should very much like to have an answer from you as quick as possible as the case is rather urgent because of the claim from Sandoz Denmark and therefore our Ministry of Health is involved .

Yours sincerely

Gro-C

Eva Sandberg