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Professor F E Preston
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Dear Eric

I am sorry we did not discuss further in Dublin your proposed application to the DOH to study the natural history of HCV in the UK.

Your proposed study is *fatally flawed* for the following reasons:

- i In order to study natural history, you need the date patients received their first infusion of unsterilised concentrate. In the UK, that was between 1960 and 1985, ie a period of 25 years (contrast HIV 1979-85). The UK database was started in 1977 and does not contain this information. Many centres did not start records of treatment until 1983 because of AIDS. In our own natural history study where we had 255 HCV seropositive individuals, we could only find date of first treatment in 183 - those who had always been at The Royal Free with the meticulous records kept by Katharine Dormandy from 1964.
- ii In individuals who have been infected with HCV PCR positivity, seropositivity to HCV and genotype vary over time. Thus such detailed analysis would only be possible where there is a longitudinal sera store - possibly only Edinburgh and The Royal Free.
- iii It is not always clear if individuals have died in liver failure, eg, in our own cohort (*Lancet* 1995; 345: 1309) in 1995 whereas 49 individuals died, the cause of death was liver failure in four, but actually nine died in liver failure.
- iv The diagnosis of HCC is notoriously difficult, even at postmortem.

Prof Preston

Thus, whilst the deaths in the UK population of haemophilic patients will continue to be monitored, they will inevitably underestimate the true size of this epidemic. For a clear understanding of the biology of HCV and the progression we will have to depend on smaller cohort studies. It is for all these reasons that I cannot support your application from The Liver Working Party to The DOH.

Yours sincerely

GRO-C

Christine A Lee

cc	Dr Chris Ludlam)	
	Dr Paul Giangrande)	Liver Working Party
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	Dr Brian Colvin		Chairman UKHCDO
	Dr Andrej Rehman		DOH