Reply. Gröner A. [Pereira A. Cryoprecipitate versus commercial fibrinogen concentrate in patients who occasionally require a therapeutic supply of fibrinogen: risk comparison in the case of an emerging transfusion-transmitted infection. Haematologica 2007; 92:846-9].

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In the previous *Online Only* article, Dr. Gröner recalculates our model[1] and concludes that commercial fibrinogen concentrate is safer than cryoprecipitate against emerging pathogens. Though he uses a somewhat different set of assumptions, the resulting odds for exposure through commercial fibrinogen relative to cryoprecipitate (631 to 1) are quite close to our estimate. However, Gröner goes further than we did and he introduces a *virus reduction factor* that renders commercial fibrinogen virtually sterile. Obviously, if one assumes that any emerging pathogen will be sensitive to the virus inactivation procedures that are currently in use, further risk analysis becomes superfluous. But asserting that coagulation factor concentrate (CFC) will be safe in the face of new, presently unknown infectious threats just because it was safe against known pathogens is intrinsically self-deceiving.

Parvovirus B19 has been found in CFC submitted to a variety of inactivation procedures, including pasteurization.[2] Levels of B19 DNA in some lots are similar to those found in the non-inactivated CFC that were marketed in the early eighties, thus showing that virus reduction may be not so effective as expected. Parvoviruses are frequent contaminants in plasma pools used for the manufacture of CFC[3] and, together with related enteroviruses, have been recognized as a potential, emerging threat to the safety of plasma-derived CFC (ref. #9 in our article)[1].

Regarding a possible pooling-mediated dilution of the new agent, as it is implicit in the computations made in the Letter to the Editor, nothing can be said for certain, but history has shown that HIV and hepatitis viruses were not significantly diluted. They even seem to have been concentrated during the manufacture of some CFC. In fact, the official position of the *British Spongiform Encephalopathy Advisory Committee* (SEAC) on the possible transmission of prions is that (I quote) 'pooling blood to dilute infectivity does not decrease the risk to public health. Indeed, depending on the dose, pooling is likely to increase the risk to public health.'[4] And the infectious dose of an emerging pathogen for which there is not yet a laboratory screening assay may be much higher than the 10^3–10^6 level assumed in the previous *Online Only* article. HIV-1 levels in plasma may reach more than 10^7 RNA copies per ml early after infection,[5] and even higher levels in some experimental conditions (ref. 11 in our article)[1], so there is nothing in our current knowledge that prevents us from thinking of an emerging pathogen reaching these or higher levels in asymptomatic donors.

We analyzed risk of exposure and made no attempt to estimate risk of infection because of the uncertainty inherent to the many intervening factors that may turn exposure into infection for an emerging, currently unknown pathogen. However, uncertainty must be taken into account when making decisions on whether to use cryoprecipitate or commercial fibrinogen for an individual patient. By quantifying the degree of uncertainty, our study tries to help physicians and patients in this decision-making. Negating uncertainty by asserting that this or that product offers absolute protection against the unknown may be a rather comfortable stance, but it is not a realistic one.

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