PPTA
Plasma Protein Therapeutics Association

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Ministerio della Salute
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Subject: Requirements introduced by decree of 19 August 2005

Dear Dr. Martini, dear Dr. De Giuli,

The Plasma Protein Therapeutics Association (PPTA) has become aware of the important new requirements introduced by decree of 19 August 2005[1]. By enforcing the European Blood Directive[2] additional measures have been set, requiring screening for ALT, Syphilis and Hepatitis C virus nucleic acid amplification technology (NAT). Apparently the scope of these measures as well as its formulation is not clear. In more detail, for Hepatitis C NAT testing it is required that each donation must test negative and no differentiation is made regarding the intended use, i.e. for transfusion purposes or further manufacturing. The measures requested go beyond state-of-the-art procedures.

The plasma protein industry is extremely concerned that this internationally unprecedented Italian requirement will have serious and perhaps unanticipated consequences with no added safety benefits for the plasma derived medicinal products manufactured and distributed by PPTA's members and comprising 100% of the plasma derivatives needed in Italy.

It is our belief that if implemented strictly this decree[1] risks the commercial viability of fractionation in Italy. In addition, because no plasma collected specifically for fractionation is currently tested in the requested manner Italian patients could be exposed to product shortages and related serious consequences. As you know, companies have already had to unnecessarily keep urgently needed plasma derivatives in inventory because of the new requirements. Fortunately for the patients, Italian authorities have exceptionally allowed release of the affected products. An industry cannot plan on the basis of such exceptions.

We understand that the continued employment of our members' highly skilled employees in Rieti and Castelvecchio can only be assured if sufficient acceptable plasma for fractionation is available. In the light of the current plasma screening

[1] Decreto Legislativo 19 agosto 2005, n. 191
[2] European Blood Directive , 2002/98/EC

policy in Europe, the new regulation would render a significant amount of plasma unusable for fractionation in Italy.

For plasma for fractionation, European regulations[3, 4] require NAT testing for HCV in production pools only. These regulations specify detection limits, levels of sensitivity, specificity and robustness and provide precise guidance on the use and validation of this sensitive technique. PPTA members have demonstrated over the last ten years that in compliance with these European guidelines/requirements HCV NAT non-reactive plasma pools can be reliably and reproducibly obtained. This could be achieved by performing the HCV NAT test on samples of minipools containing 500 samples or more.

It is universally accepted and unchallenged that plasma pools complying to the above mentioned European regulations are suitable to be fractionated into safe and efficacious plasma products.

In view of these serious consequences for the viability of the Italian based industry, PPTA's interest on behalf of our members is to convince you that the only way to avert this situation is to proceed in line with the European Blood Directive and with practices accepted internationally and by every other EU Member State. We are advised that the decree mentioned above[1], the related Italian decrees and the European legislation from which it is derived, provide the necessary flexibility for a different interpretation and approach to the testing of plasma for fractionation.

A fresh interpretation is necessary in order that our industry can ensure that Italian patients' have sustained access to the therapies on which they depend. PPTA and its members are committed to work with you, other Italian experts and appropriate international experts to help resolve this situation expeditiously and without any reduction in the final quality and safety of the life-saving medicinal products manufactured by our members.

Sincerely yours,

Charles Waller
Executive Director

[3] The Introduction of of Nucleic Acid Amplification Technology (NAT) for the detection of hepatitis C Virus RNA in Plasma Pools, CPMP/BWP/390/97
[4] Nucleic Acid Amplification Techniques, European Pharmacopoeia 01/2005:20621 corrected