Plasma Protein Therapeutics Association

26 March 2009
Reference: EMEA 09006b

EMEA PMF Epidemiology Workshop with Industry, 30 and 31 March 2009

Submission of Epidemiological Data, Bernhard Lauven

PPTA has experience with central viral marker reporting for a long time in the context of the IQPP program, a voluntary initiative which was implemented in 1991 in the US and in 2000 in Europe. The central viral marker reporting provides the opportunity to address data quality and data integrity issues and the basis for analysis of industry-wide collections data. However, IQPP data collection is restricted to source plasma centers of PPTA members.

The experience with the IQPP data collection points to some of the difficulties regarding the statistical analysis: the data are spread over a wide range and there are low absolute numbers at the center level, thus often requiring "sophisticated" statistical models.

The collection of data according to the EMEA guidance raises additional issues, specifically for the definition of true "incidence" and "prevalence". These difficulties are already acknowledged in the EMEA/CHMP guidelines by suggesting an approximation. To obtain the information in Section 5.2 for repeat tested donors requires the center to go back two years to ascertain donor status or to identify those with evidence of recent infection by laboratory or clinical data. PPTA believes that using a "positivity rate" could be a more appropriate term, as it would provide for a "worst case" assumption and prevalence is more accurately assessed than incidence. However, the issue of approximation of "true incidence" in the donor population remains unsolved. This is even more significant for recovered plasma, because donations from first time tested donors are used. Here some assumptions must be made on the relationship between first-time donor positivity and incidence to derive an incidence estimate. Furthermore, the interpretation and analysis of the data is difficult, because comparison of the donor population to the general population is neither feasible nor meaningful and no metric for comparison currently exists. Statistical analyses need to take into account the low absolute numbers of positive donors at the center level. An increase in the positivity rate at the center level in one given year has to be interpreted cautiously and correctly, i.e. the possibility of chance occurrence has to be considered. Also the trending and the interpretation, respectively, are difficult, due to the limited database of 3 years only, which opens the possibility of "artefacts".

For example, PPTA has performed a statistical analysis on industry US qualified donations and viral positivity rates per 100,000 donations for HIV, HCV and HBV by year in 2008 for the time period of 2003-2007 to discern whether the level of differences between any two years' data was significant and whether the difference represented a trend. No statistical difference between any two years was observed (95%CI), neither was a trend detected in any marker rate over time. In no instance did any individual year exceed the upper confidence level, i.e. no significant deviations from the mean occurred.

PPTA would like to suggest using a positivity rate instead of an incidence rate. It needs to be taken into account that the comparison of data for 3 previous years is difficult and hard to interpret. Limited trending analysis has scarce value for evaluating the donor population

Boulevard Brand Whitlock, 114/5 · 1200 Brussels BELGIUM · tel : +32.2.705.58.11 · fax : +32.2.705.58.20
VAT: BE453 837 462 · e-mail: pptaeu@pptaglobal.be · www.pptaglobal.org
PPTA Offices in Brussels · Washington · Annapolis · Tokyo

at specific centers. PPTA believes that it is most important that collection centers stay within a defined acceptable range for quality control purposes, which at this point of time has not yet been established. This lack of a reference range may potentially lead to different interpretations by various viewers. Therefore, in the interest of all involved parties, and specifically in the interest of patients in need of these often life saving therapies the most important tool is a viral marker rate standard with alert/action levels acceptable and practicable for all stakeholders.