

March 10, 2008
Reference No.: SASC08023

VIA FEDERAL EXPRESS

Ms. Virginia Herold
Executive Officer
California Board of Pharmacy
1625 N. Market Blvd, N219
Sacramento, CA 95834

Dear Ms. Herold:

On behalf of the Plasma Protein Therapeutics Association (PPTA), I am writing to request that you exercise your statutorily granted discretion as codified in the California Business and Professions Code and delay implementation of the substantive aspects of California's Pedigree requirements until January 1, 2011. CAL BUS. & PROF. CODE § 4163.5 Patients that rely upon life-saving plasma-derived and recombinant analog therapies (collectively, "plasma protein therapies") cannot risk any disruption to their access to care. In this instance erring on the side of caution by delaying implementation and putting access to care first for the chronically ill patient populations treated with plasma protein therapies should be paramount. We reiterate our comments in our letter dated December 19, 2007 and also want to make the Board of Pharmacy aware of additional reasons that prevent the plasma protein therapeutics industry from meeting the January 1, 2009 deadline.

First is the uncertainty of Radio Frequency Identification technology (RFID) on biologics. This issue was discussed briefly at the January 23, 2008 meeting. We know that no commitment has yet been made to RFID technology. Nevertheless, we bring this issue forward in the interest of having a full and complete dialog about the unanswered questions surrounding pedigree implementation. Second, we would also like to address the requirement prescribed in the Food and Drug Administration Amendments Act of 2007 (FDAAA) which calls for, within 30 months of enactment, the development of a standardized numerical identifier that will be applied to a prescription drug at the point of manufacturing and prepackaging at the package or pallet level, sufficient to facilitate the identification, validation, authentication, and tracking and tracing of the product. Finally, the implementation of any statute should take into account the global impact it could have on access to therapies.

PPTA is the primary advocate for the world's leading producers of plasma-derived and recombinant analog therapies. PPTA global member companies include Baxter BioScience, Biotest, Talecris Biotherapeutics, CSL Behring, Grifols Inc., Kendrion, and

Octapharma USA. Plasma protein therapies, which include albumin, blood clotting factor, alpha-1 proteinase inhibitors and intravenous immunoglobulin, among others, are life-saving therapies used to treat a variety of rare diseases and serious medical conditions for a very small, often compromised patient population in the United States. The complexity of biologics must be taken into account when considering a law directed at comprehensive prescription drug distribution. PPTA members are committed to ensuring the safety and availability of these medically needed life-sustaining therapies.

The United States Food and Drug Administration (“FDA”) has found that counterfeiting of medications is a particularly insidious practice. Thus, the need to prevent this through the use of RFID or other track and trace technologies within the pharmaceutical supply chain was strongly suggested by the FDA.¹ In addition, the FDA issued guidelines for manufacturers and others who wished to perform feasibility studies on the use of RFID for tracking prescription and over-the-counter-drugs.² Among other things, these feasibility studies were intended to determine potential negative impacts of such technologies on the safety and efficacy of drugs and biologics. PPTA member companies take the issue of counterfeiting very seriously and have instituted safeguards to ensure that the potential risk of counterfeiting is minimized.

In 2005, FDA recognized that the potential effects of RFID on biologics were uncertain. FDA stated that studies were needed to obtain a better understanding of such effects. Subsequently, the FDA developed a protocol to test the potential impact of RFID technology on drugs and biologics.³ The protocol was developed to enable studies of the effects of certain radio frequency electromagnetic fields on solid and liquid pharmaceuticals and biologics in their primary (retail) packaging and in culture dishes. The exposure fields produced by the systems were similar to those emitted by RFID systems that will be used to read special labels placed on prescription drugs. The exposure systems can be used to study possible adverse effects on drug safety and effectiveness produced by RF fields. The fields are higher than those produced in typical systems but the protocol was designed to assess so-called “worst-case” scenarios. When crafting the protocol, discussions between FDA and RFID industry representatives revealed that a drug product’s RFID tag may need to be situated as close as 20 cm from a commercial, stationary RFID reader. Therefore, the system was designed to expose drug products (at 20 cm) to at least 5 times the maximum allowable UHF Effective Isotropic Radiated Power (EIRP) in the USA produced by UHF commercial readers. PPTA member companies agreed to participate in these studies by supplying products for use by FDA.

Previous studies on the biological effects of HF and UHF electromagnetic fields on animals and cell cultures have indicated that imposing low-frequency amplitude modulation (e.g. 60 Hz) to a continuous wave (CW) RF signal was a critical factor in

¹ H. Bassen, et al., *An Exposure System for Evaluating Possible Effects of RFID on Various Formulations of Drug Products*, presented at the IEEE International Conference on RFID, March 2007.

² *Id.*

³ *Id.*

causing changes.⁴ It is recognized that certain materials found in biologics have the potential to interact with electromagnetic waves emitted by an RF source more than others. Perhaps, upon localized, prolonged RF exposure, and through an unintended arrangement of units in a bulk carton, a measurable adverse effect could be produced in one of the carton's members. Thus, it is conceivable that if a group of conditions are met RF exposure could compromise a biologic product.

At the present time, FDA has not released the results of their study on the potential impact of RFID on biologics. One important takeaway from the study however, is that we should proceed with caution. On October 12, 2007, FDA expressed concern to PPTA regarding the limitations of the study. In particular, FDA acknowledged that only one type of plasma protein therapy had been tested and that each therapy has its own unique properties which could be impacted by RFID. FDA also stated that some dimers and aggregates formed within the products tested but they still remained within their specifications. Furthermore, FDA emphasized that the study did not provide information to determine the long term effects of RFID and that more studies should be undertaken to address this issue. Accordingly, there are numerous unanswered questions about the potential impacts of new track and trace technologies on biologics. Additional testing of these effects could take place during the delay in implementation. Again, we believe that maintaining the safety of the therapies manufactured by our member companies is paramount. To that end, we assert that further testing of the various technologies is necessary to show conclusively that they will not have unintended effects upon the safety and efficacy of the therapies manufactured by PPTA member companies.

On September 27, 2007, President Bush signed into law the FDAAA. As stated above, FDA is required to develop a standard numerical identifier (SNI) by 2010. PPTA spoke with representatives from FDA and learned that they have initiated preliminary work on the development of a SNI. Under the law, the standards developed by FDA may include radio frequency identification technology, nanotechnology, encryption technologies, and other track and trace or authentication technologies. PPTA is concerned that incompatible standards initiated at the state and federal level will cause disruptions in the supply chain. It may also result in redundant requirements that do not further secure the supply chain. If the California requirements are not delayed to allow FDA the time to develop a federal standard, an undue burden might be placed on America's drug supply chain, potentially compromising consumer access to therapies.

Lastly, it is imperative that the standards developed for the tracking and tracing of drugs be compatible with international requirements. Congress recognized the importance of global harmonization and requires FDA take this into consideration as they develop the SNI. For example, the European Federation of Pharmaceutical Industries developed packaging standards, which includes the recommendation to use two-dimensional bar

⁴ *Id.* Citing Penafiel, L "Role of Modulation on the Effect of Microwaves on Ornithine Decarboxylase Activity in L929 Cells," BIOELECTROMAGNETICS, Volume 18, Issue 2, 1998.

codes. Japan has developed elaborate label and serialization requirements. As the U.S. moves forward with serialization requirements for track and trace, a complete understanding of international standards is necessary to ensure that superfluous regulatory barriers do not inhibit patient access to life-saving therapies.

PPTA greatly appreciates the opportunity to comment on the implementation of the California pedigree law. PPTA hopes to be part of the dialog with the Board as it continues to work with the issues associated with implementation of this important law for the residents of California. Should you have any questions, or if you require additional information, please do not hesitate to contact me at (202) 789-3100 or by email (rfaden@pptaglobal.org).

Very truly yours,



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