groups have investigated a range of methods to modify this burst release, but to date no product with an altered release profile has made it to market.

Secondly, due to the issue of the stability of PLGA in NMP, the Atridox® system is only available as a two component system that must be mixed prior to use by a trained individual. This can be a lengthy process and is obviously not ideal. A two-component system could therefore be detrimental in terms of progress towards a patient self-administered formulation. Some work has been completed to combat the issue of PLGA instability in the form of alternative solvents. It has been shown that PLGA stability is increased when formulated in end-capped PEGs and the resultant solvents (PEG500DME and PEG-DAE) have shown favorable release and toxicity profiles (Schoenhammer et al. 2009a; Schoenhammer et al. 2009b).

Due to conflicting data relating to the toxicity of these ISFI, this area is still of concern to research groups and may be limiting their use in practice. The main concern relates to the use of organic solvents. The consideration of other solvents has resulted in ethyl benzoate and low molecular weight PEGs being shown to be compatible (Kranz et al. 2001). As stated previously, Schoenhammer et al. have shown the promise that lies with end-capped PEGs for use in these systems (Schoenhammer et al. 2009a; Schoenhammer et al. 2009b). Currently, there are no marketed or near to market systems that fulfill the criteria of an ideal ISFI but this is an area that is rapidly moving and research is growing.

Conclusion

In situ forming systems are gaining significant interest among pharmaceutical and biotechnology industries to formulate control drug delivery applications—particularly, due to enhanced patient compliance and simple administration procedure. *In situ* forming SPI implants has unique advantages over other forms of ISFI as sustained release systems such as thermo, pH, and ion responsive systems. These systems have many inherent advantages such as ease of production, biocompatibility of components, controlled release profiles and also the accommodation of both hydrophilic and hydrophobic drugs for delivery. However, as mentioned previously, solvent-induced ISFIs are not without their drawbacks. These implants are currently susceptible to burst release meaning that levels of drug above the therapeutic range may be released in the first 24 hours after implantation, possibly resulting in toxicity-related adverse effects. Also, there is conflicting information relating to the use to organic solvents and their toxicity within the body therefore there is a pressing need for alternative, non-toxic solvents for use in these systems. Issues relating to stability of polymers, such as PLGA, in organic solvents have resulted in those systems currently available on the market being produced as two-component systems that require extensive mixing prior to use. This may cause problems if mixing instructions are not stringently adhered to resulting in a non-homogenously mixed system that is injected. Due to the issues underlined, as of yet, there are a limited number of products on the market utilizing this promising technology therefore efforts must be made to produce commercial products that will benefit patients worldwide.