changes and chemical agents (Gil and Hudson 2004). Physical stimuli include electrical fields, temperature, solvent changes, light, pressure, magnetic fields and pressure.

A stimuli responsive system has a number of distinct advantages over conventional polymeric delivery systems, depending on the type of polymer. Those systems that once exposed to a stimuli experience a sharp rise in viscosity are initially of low viscosity and therefore allow easy administration through a syringe. A system that gels, or is triggered to release drug particles, once exposed to a change in pH can result in targeted drug delivery. As well as in drug delivery, stimuli responsive polymers are being utilized in a number of different fields such as aerospace, textiles, sensors, microfluidics, bioengineering, packaging and actuators (Lendlein and Shastri 2010).

In Situ Forming SPI Hydrogel Implants

This aims to discuss the SPI-based ISF hydrogel implant technology, which has attracted significant attention among pharmaceutical/drug delivery companies, leading to the development of commercial therapeutic products for a wide range of clinical applications. Importantly, SPI mode of ISF implants has a number of advantages over its counterparts, e.g., need for critical temperature (for thermoresponsive ISF implants), presence of ions (for charge sensitive ISF implants), and change in pH (for pH sensitive ISF implants) is not required to trigger implant formation. Therefore, considering the growing interest in SPI type ISF drug delivery systems, this work critically assessed the literature available in relation to SPI hydrogel implant technology.

SPI is known by a number of different terms throughout published literature, namely, non-solvent induced phase separation (NIPS) (Wang et al. 2004), solvent exchange (Ruel-Gariépy and Leroux 2004), solvent/non-solvent exchange (Kranz and Bodmeier 2008), solvent removal (Hatefi and Amsden 2002; Chitkara et al. 2006), liquid-liquid phase separation (Brodbeck et al. 1999a), solvent-removal precipitation (Dong et al. 2011), polymer precipitation (Packhaeuser et al. 2004; Körber and Bodmeier 2008) and phase-sensitive ISFIs (Yu and Singh 2008). This method of implant formation *in situ* has numerous benefits compared to its counterparts mentioned above. For example, control of temperature is not an issue, which is in contrast to those systems that require a critical temperature for gelation to take place. Also the application of an external energy source, such as a UV light, is not required (Hatefi and Amsden 2002). These systems first came into existence through the work of Richard Dunn and colleagues at the Southern Research Institute in the 1990s (Dunn et al. 1990).

SPI hydrogel systems are comprised of a water insoluble polymer that is dissolved in an organic, water-miscible, biocompatible solvent, into which a drug is incorporated. Once this system is introduced into aqueous environment, the organic solvent dissipates out of the system and water ingress via diffusion (Graham et al. 1999). This exchange of solvents results in sol-to-gel transformation causing polymer precipitation that leads to hydrogel implant formation, which in turn controls the rate of drug release.

Effect of polymer type

The body of knowledge relating to phase inversion is vast and this has led to the investigation of a number of polymers for their potential to form ISFI (Brodbeck et