USA (subsequently acquired in 2010 by Allergan, Inc.) using technology originally developed by David Kaplan and co-workers at Tufts University, MA, USA. Data from two clinical trials with these surgical meshes have been encouraging, with high levels of investigator and patient satisfaction scores and no adverse reactions due to the silk mesh (De Vita et al. 2014; Fine et al. 2015). Early phase trials are currently ongoing to test BioShield-S1 silk coatings of silicone breast implants to improve host–tissue responses [based on eADF4(C16) spider silks manufactured by AMSilk, Munich, Germany]; these clinical studies were preceded by successful *in vivo* studies that showed no acute systemic toxicity and immunogenicity with eADF4(C16), as well as a significant reduction in capsule formation with the silk-coated silicon implants (Zeplin et al. 2014). In particular, the successful track record of silk sutures for use in humans has served as the launching platform for the development of silk-based materials for biomedical applications, including cell and drug delivery.

Biocompatibility

Nonetheless, the generic use of the term "biocompatibility" to describe silks is potentially misleading. In particular, the notion that any natural material automatically qualifies as biocompatible is widespread but misleading, with potentially disastrous consequences. For example, some of the most toxic compounds known to man are of natural origin (e.g., botulinum toxin). When used clinically and for aesthetic purposes, both the dose and route of administration are critical for safe use. Therefore, all (bio)materials need careful assessment prior to their *in vivo* use. The biocompatibility definition by David Williams "refers to the ability to perform as a substrate that will support the appropriate cellular activity, including the facilitation of molecular and mechanical signalling systems, in order to optimise tissue regeneration, without eliciting any undesirable local or systemic responses in the eventual host" (Williams 2008). Although silk has a proven track record in humans as a suture material, context specific biocompatibility assessment is still required when silk is being used beyond its licensed applications. For example, silk has been proposed for various vascular tissue engineering applications, but without first undergoing rigorous haematocompatibility assessment. We have assessed the blood compatibility of silk and were able to demonstrate a low haemostasis activity but an inflammatory response that was in part dependent on the processing history of the silk (Seib et al. 2012; Seib et al. 2014).

Silk biocompatibility

In vivo studies in rats indicated that silk films implanted intramuscularly induced a mild inflammatory response, appearing in the form of fibroblasts, few new blood vessels and macrophages at the implant-host interface. This type of tissue response was more noticeable for polylactide and collagen films at 6 weeks post implantation than for silk films (Meinel et al. 2005). The silk scaffolds also showed different *in vivo* degradation behaviour depending on whether they were generated by water- or solvent-based processing. For example, water-based silk scaffolds with large pore sizes (850–1,000 μm) were completely degraded and resorbed within 6 months,