In summary, our initial proposition was that if we are to advance in the design of polymers to
interface with and mimic biological systems, we need to develop responsive polymers [3.1]. This underpinning concept has already been successfully applied to soft contact lens surfaces that mimic aspects of the corneal behaviour (Section 4A) where the claimed impact is well-established. The significance of BRU research in the biomimetic design of soft tissue analogues was recognised by: the inaugural award of Inaugural UK Society for Biomaterials Presidents Prize (2002), the BCLA Gold Medal (2003), and the IOM Chapman Medal for innovation in biomaterials (2006).

### 3. References to the research (the 3 marked * are best indicators of research quality)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Title and Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2 *Oxley HR, Corkhill PH, Fitton JH and Tighe BJ.: Macroporous hydrogels for biomedical applications: Methods and morphology, Biomaterials 1993, 14:1064-1072. doi.org/10.1016/0142-9612(93)90207-I</td>
<td></td>
</tr>
</tbody>
</table>

This underpinning research has been supported by both BBSRC (e.g. “An integrative approach to the development of a novel biomimetic keratoprosthesis”, £188,675, 01/02/1999) and EPSRC (e.g. “New Clinical Materials for Biomimetic Repair of Intervertebral Disc”, £247,411.00, 24/07/2003) through peer-reviewed research grants. Results were published (e.g. 3.2) in the leading (web of science) biomedical materials journal with an invited overview (3.1) in a 14 impact factor journal.

### 4. Details of the impact

**The business and health benefits**

**A) RESPONSIVE MACROMOLECULAR RELEASE: A PLATFORM FOR MORE COMFORTABLE CONTACT LENSES**

BRU research is regularly presented to the mixed commercial, clinical and academic audience at the annual Clinical Conference of the British Contact Lens Association (BCLA) by Tighe and co-workers. The relevance of BRU work to both UK and US ophthalmic industry and clinical community is reflected in the reporting of such presentations on websites sponsored by major companies. [e.g. 5.1] Through this mechanism the commercial and clinical relevance of BRU work is recognised. The development of a series of daily disposable contact lenses [5.2] (e.g. CIBA DAILIES™ All Day Comfort™ and CIBA DAILIES™ Aqua Comfort Plus™), which incorporate the concept of blink-activated release of linear polyvinyl alcohol by a reptation mechanism, arose from this process. The consequent corneal mimicry dramatically reduces the end of day discomfort that limits the wear duration of the unmodified lens.

CIBA personnel [5.10] first became aware of, and identified the importance of BRU research,
through reference [5.10c] presented at the 1998 BCLA conference. Following a visit to BRU where the blink activation process and its potential enhancement in PVA-containing lenses was explained, CIBA began to embody the principles in their products. In consequence CIBA made unrestricted research donations to BRU which for a ten year period supported a PDRA working on ocular biomaterials research at Aston.

The more recent CIBA product variant (CIBA DAILIES™ Aqua Comfort Plus™) uses two polymers (polyvinyl alcohol and polyethylene glycol) within the lens matrix and a third surface-active polymer added to the lens packing solution. BRU has developed unique methodology demonstrating the in-eye duration and effectiveness of such surface-active polymers adsorbed onto the lens surface [3.4]. The CIBA DAILIES™ products couple this mechanism with blink-activated release of polymers from the lens matrix. The release mechanism that we proposed is incorporated in a marketing claim that the lens “moisturises at every blink” [5.2].

The latest DAILIES product (launched 2012) is a silicone hydrogel lens known as DAILIES Total 1™. This product contains phosphatidylcholine; intended to be ocularly released; so as to stabilise the aqueous tear film. This contribution, too, can be directly attributed to BRU influence and supporting research. In fact, CIBA VISION has sought out BRU assistance in pre- and post-market support in this arena [5.10].

BRU’s research in identifying and quantifying the blink-activated release of polyvinyl alcohol, and the mechanism of macromolecular modification of the lens surface has had significant health and commercial impacts. It underpinned the blink activation principle, which now characterises all CIBA DAILIES™ lenses, sold in more than 70 countries with an annual ‘DAILIES’ PVA-only production (2011) of over 2 billion lenses [5.4]. CIBA has a market share of ca 25% of the worldwide contact lens market, now estimated at $6.8 billion. Daily disposable lenses account for 15% of lenses fitted, but almost 35% of soft lens revenue [5.3, 5.4]. CIBA Vision has recognised BRU’s contribution in presentations and publications and key CIBA personnel involved will provide verification “to any review panel” [5.10].

**(B) RESPONSIVE GAG MIMICS IN OCULAR, ORTHOPAEDIC AND DERMAL APPLICATIONS**

Ongoing biomimetic design of other soft tissue GAG analogues has included a long-term relationship with SME, First Water Ltd, a specialist UK manufacturer of wound dressings, skin adhesives and conductive hydrogels. Commercial outcomes were recognised by EPSRC via their national Knowledge Transfer Challenge competition and this impact that has continued throughout the impact period, was described (archived EPSRC website) as first-class interaction between researchers and industry [5.5].

A novel intervertebral disc application involves an injectable pre-gel avoiding the need for major surgical intervention and, by mimicking the natural GAGs, restores osmotic responsiveness and disc height. The exploitation potential of the fundamental work (Section 3) was recognised by an EPSRC “follow-on” award, given to develop IP and subsequent commercialisation [5.6]. The novelty of the resultant patent [5.7] was recognised in the US “Best Spine Technologies of 2009” awards by the US orthopaedics industry journal, Orthopaedics This Week, where it was highlighted as one of the top three regenerative spinal technologies of the year [5.8]. Long-term studies of biomechanical stability are in progress.

BRU studies of the application of responsive GAG analogues to therapeutic and cosmetic contact lenses for dry eye symptomatology, including a process development programme, supported by J&J Vision Care has led to joint intellectual property [5.9].

During the impact period there have been further awards to Prof Tighe, recognising the significance and commercial importance of BRU achievements, including the European Contact Lens Industry (EFCLIN) Technology Award (2008) and the ISCLR (predominantly funded by the international contact lens industry) Research Medal (2009).
5. Sources to corroborate the impact

5.1 http://www.thevisioncareinstitute.co.uk/sites/default/files/content/uk/doc/111215%20TVCI%20Assottica.pdf.

5.2. Advance to DAILIES® brand contact lenses
   The only contact lenses with blink-activated moisture (accessed 14th May 2012): http://www.dailies.com/for-ecp/for-ecp-technology.shtml

   DAILIES® AquaComfort Plus® Contact Lenses
   Brand new lens every day, refreshing all day (accessed 14th May 2012): http://www.dailies.com/products/dailies-aquacomfort-plus.shtml

5.3 Contact Lenses 2011: Market and survey data


5.5 Faster and more effective treatment for wounds - an example of first-class interaction between researchers and industry. EPSRC March 2007 (accessed 14th May 2012): http://www.epsrc.ac.uk/newsevents/casestudies/2007/Pages/wounds.aspx

5.6 12 month EPSRC Follow-on grant: Clinical Materials for Biomimetic Repair of Intervertebral Disc, Value £259K
   Awarded to Prof B. J. Tighe (EP/G006202/1) Start date October 2009


5.8 Orthopaedics this week


5.10 The former Global Head R&D Strategy and Business Alliances (LCW), and Global Head of Research (JML), CIBA VISION (now Alcon CIBA) principal authors of the CIBA publication (a) below "will be happy to validate all of this information to any group or review board". [email addresses placed on file].

   CIBA publication (b) explicitly presents the original CIBA assertion that was challenged by the BRU research, first reported in publication (c) that led to the claimed impact. Reference (c) is a pdf provided by the former CIBA Global Head of Research showing the poster annotated with JML’s first circulation of the information with CIBA Vision. References (a-c) were suggested by CIBA personnel LCW and JML as corroborations of the route to impact.

