# Re-Profiling: a Hidden Threat to Originators?

## Contributory Infringement of Second Medical Use Claims

Dr Jo Davies, August 2010

As James Black is famously quoted as saying, "the most fruitful basis for the discovery of a new drug is to start with an old drug". This has stimulated a heightened search for new indications for already-known drugs, also known as drug reprofiling. For venture capital investors, it takes too long and costs too much to bring new drugs to market, but the "de-risked" opportunities of reprofiling can appear attractive. What is little appreciated, however, is that third-party drug reprofiling activities can, under certain circumstances, pose threats to the marketer of the original drug, even if the original patents have expired. This risk is due to the concept of Contributory Infringement (see Box below for definition), and the following paragraphs set out an illustrative scenario.

**Contributory Infringement**

A person (other than the proprietor of the patent ) infringes a patent for an invention if, while the patent is in force and without the consent of the proprietor, he supplies or offers to supply a person other than a licensee or other person entitled to work the invention with any of the means, relating to an essential element of the invention, for putting the invention into effect when he knows, or it is obvious to a reasonable person in the circumstances, that those means are suitable for putting, and are intended to put, the invention into effect.

### SPIDER VENOM SCENARIO

#### Background (FACT)

The six-eyed sand spider (Sicarius) of Southern Africa is considered to be the world's most venomous spider. Spiders of this family posses a venom containing sphingomyelinase D; bites from these spiders may form a necrotising ulcer that destroys soft tissue. Severe systemic symptoms include haemolysis, thrombo-cytopenia and disseminated intravascular coagulation (DIC). In DIC the blood starts to coagulate throughout the whole body, depleting the body of platelets and coagulation factors and leading to the paradoxical situation in which there is a high risk of catastrophic thrombosis and simultaneous massive haemorrhage.

#### First Medical Use of Spider Venom (FICTION)

The original indication, or first medical use, is as a treatment for the rare type of blindness known as Shuttle's "Red-Eye". In Red-Eye, blood leaks into the vitreous humour of the eye and obscures vision. An injection of spider venom (SV) directly into the eyeball causes coagulation of blood and removes any suspended platelets, without causing other side effects. There is a risk of severe eye damage if the SV comes directly into contact with any soft tissue surrounding the eye, and so it must be injected very carefully and in a controlled dosage. SV is collected and sold in lyophilised form in individual ampoules by the Originator company.

#### Second Medical Use of Spider Venom (FICTION)

The patented second indication is as a cosmetic treatment for reducing or removing skin blemishes, birthmarks and the like. An injection of SV just under the epidermis at the interface between the upper dermal layer and the lower epidermal layer. The necrotic and haemolytic effect is localised and because the epidermis is

avascular, the SV does not exhibit a systemic effect. There is a risk of tissue damage if too much SV is used and it leaks into the lower dermal layer. SV is collected and sold in lyophilised form in individual ampoules by the Reprofiler.

**Originators Dilemma**

Originator supplies small quantities of SV to specialist physicians for treating the rare disease Red-Eye. Originator knows that its SV can be used for the new cosmetic indication, and is aware of the serious potential health risks for misuse because the dosage needs to be controlled.

Reprofiler supplies SV widely for the cosmetic treatment. Given the level of Reprofiler's promotion of SV, Originator may gain collateral benefit in terms of sales of its SV. Of course, Originator cannot know for certain what each person might intend to do with any Originator SV they acquire.

What can Originator do to reduce or eliminate the risk of being held to be a contributory infringer?

**Key Questions**

- If a doctor asks Originator for documentation relating to the use of SV in cosmetic treatments, can Originator provide it?
- Is there a moral, ethical or legal obligation or duty for Originator to mention potential adverse consequences which might occur if there is misuse of SV in cosmetic treatments?
- Can Originator publish its own articles/papers which mention that its SV is suitable to be used in cosmetic treatments, if the authors draw attention to the fact that the new use is patented?
- Can Originator make oral presentations which mention that its SV is suitable to be used in cosmetic treatments, if the speakers draw attention to the fact that the new use is patented?
- In documentation provided to doctors with regard to use of SV in Red-Eye, can Originator:
  - state that SV is suitable for use in cosmetic treatments while drawing attention to the fact that the new use is patented?
  - provide copies of articles/publications that relate to the new indication, either with or without further explanation?
  - make reference to articles/publications that relate to cosmetic treatments without providing copies?
- Is there any action which Originator needs to take if it finds that a third party has published an article/paper on the use of SV in cosmetic treatments, and the author indicates that the SV was obtained from Originator?

**Does it make any difference if:**

- The SV supplied by Originator and Reprofiler respectively does or does not contain the same concentration of active venom per dose?
- The SV supplied by Originator and Reprofiler respectively does or does not require the user to make up the injection in a use-specific medium (for example different buffers for different medical uses)?
- The supply of SV is controlled by Regulation (prescription only) or is available OTC (over the counter)?
- The cosmetic treatment is a Licensed indication, or if the doctors are prescribing for an "off-label" indication?
- Originator is asked to sell to an existing customer or a new customer?
- Originator is asked to sell an increased quantity to an existing customer?

### It's not what you do, but the way that you do it

There are no existing international agreements on contributory infringement. Most jurisdictions have a prohibition of contributory infringement but these may be interpreted differently by different national Courts. It is difficult to apply an absolute measure of liability for infringement where the alleged infringer's state of mind may be the deciding issue. An otherwise perfectly legitimate provider of a product may be at risk of becoming a contributory infringer simply by being passive, or by taking positive steps to facilitate correct use of his product: potentially the Originator can be "damned if he does, and damned if he doesn't".

A legitimate provider of a product who feels a duty to discourage or prevent or warn against infringement may nonetheless be at risk of being a contributory infringer. Allegations of objectionable intent may be difficult to prove, but they are relatively easy to make, so legitimate providers may become at risk as soon as a patent is granted for a second indication. The aims and intentions behind an alleged infringer's conduct will count for a great deal in deciding whether or not he is liable.

### Afterword

Perhaps the "fair" way to deal with this would be to encourage national Courts to differentiate between two types of potential contributory infringers in determining the threshold for a finding of contributory infringement of a Second Medical Use claim:

- a higher threshold where the supplier has already an established legitimate market and therefore has a "legitimate prior user right", and
- a lower threshold where the supplier has no prior use of the product in a legitimate market, and is entering the market to exploit the new use disclosed by the second indication.

*Further reading*

**UK case law**

Innes v. Short & Beal 1898 RPC XV, No.18 p449
Supply of zinc powder for a patented corrosion prevention method (infringed)

Dow Chemical v. Spence Bryson 1982 FSR 598
Supply of latex glue for making foam-backed carpets by a patented method (infringed)

CBS v. Amstrad, House of Lords, 1988 RPC 567
Sale of high-speed audio tape copier systems – facilitating home taping and copying (copyright not infringed – legitimate alternative use)

Bristol-Myers Squibb v. Baker Norton & Napro "Taxol" 2001 RPC 1
Second medical use claim invalid – infringement not decided

**German case law**

"Hydropyridine" Federal Supreme Court of Justice 1983, case X ZB 4/83: OJEPO 1/1984, pp26-41
Scope of protection of medical use claims extends to the packaging and instructions

**Netherlands case law**

General Hospital v. Air Products District Court of the Hague, 16 Feb 2000
No evidence of advertising the prohibited use or incitement to infringe

**US law**

US Patent Law statute 287(c)
From 30 Sept 1996 : medical practitioners exempted from infringement of patented surgical methods and medical procedures (but not exempted from infringement of methods of treatment using medicaments)

**Other**

"Creeping through the back door" – General overview on contributory infringement, Oliver Bancherau, Patent World issue 199 Feb 2008

**Spiders**

Spiders having medically significant venom
http://en.wikipedia.org.wiki/Spider_bite