Institution: University of Reading

Unit of Assessment: UoA 5 Biological Sciences

Title of case study: Parabens in personal care products: providing marketing tools for industry, informing European policy and raising public awareness

1. Summary of the impact

Governments, industry and the public have benefitted from research on the potential role of parabens, which are used widely as preservatives in personal care products, in the development of breast cancer. The research, conducted at the University of Reading since the 1990s, has established the oestrogenic activity of parabens in human cells, confirmed and quantified the presence of parabens in human breast tissue and established that parabens can stimulate the proliferation of human breast cancer cells at concentrations measured in the breast tissue. The findings of this research have received widespread media coverage, which has raised public awareness of the issue. As a result, producers and retailers of natural and organic cosmetic products have benefitted through the adoption of these research findings into marketing information available to their customers. Scientific Committees have used the research findings to inform their opinions on the risk of parabens that have been submitted to the European Commission. As well, non-government organisations have benefitted from having scientific evidence to support their public awareness initiatives and campaigns to invoke change in policy.

2. Underpinning research

Research conducted at the University of Reading since the 1990s has helped to establish a link between the chemical constituents of underarm cosmetics and breast cancer. Dr Philippa Darbre, Reader in Oncology (2009-current; previously Senior Lecturer from 2002 to 2009 and Lecturer from 1991 to 2002), conducts research on how oestrogen and oestrogen-mimicking compounds affect the development, growth and progression of breast cancer cells at the cellular and molecular level. Her research had demonstrated that some environmental chemicals, which can enter human breast tissue via the food chain, have oestrogenic and tumour promoting activity and therefore may play a causal role in the development of breast cancer [Nesaretnam, Corcoran, Dils, Darbre (1996) *Mol Endocrinol* 10: 923-936; Nesaretnam, Hales, Mohammed, Krausz, Darbre (1998) *Eur J Cancer* 34: 389-393.].

Proposal of a new hypothesis:

Darbre's expertise in the effects of oestrogenic chemicals on breast cancer cells led her to question whether the chemical constituents of heavily used underarm cosmetics, namely deodorants and anti-perspirants, had the potential to be cancer-causing. In 2001, she published a new hypothesis suggesting a link between the chemical constituents of underarm cosmetics and breast cancer [1]. She drew upon published evidence of others that showed a disproportionately high incidence of breast cancer in the upper outer quadrant of the breast, which is the region closest to the site of underarm cosmetic application. Darbre also highlighted evidence that an increase in the prevalence of breast cancer in this region coincides with an increase in the use of underarm cosmetics over the past century. Recent evidence at the time also showed that parabens, commonly used as preservative in cosmetics, mimic the action of oestrogen and are capable of penetrating animal skin. This was the first time these findings from different areas of research had been pulled together to articulate a potential link between underarm cosmetics and breast cancer.

Establishing oestrogenic activity in humans:

Although the oestrogenic activity of parabens had been shown in yeast cells and animal models, it had not yet been established in humans. Between 2002 and 2005, Darbre and her colleagues defined, over four separate papers, the oestrogenic actions of six chemical compounds commonly used in cosmetics as preservatives. They described the ability of these parabens to bind to oestrogen receptors, regulate oestrogen-responsive gene expression and increase proliferation in oestrogen-responsive human breast cancer cells, thereby demonstrating their oestrogenic effects in human cells [e.g., 2].

Measuring parabens in human breast tissue:

Though Darbre and her colleagues had established the oestrogenic effects of parabens in human cells, it remained unclear whether these compounds could accumulate intact in the body as a

result of long-term, low-dosage use such as daily application of cosmetics. In a collaboration with colleagues at The Edinburgh Breast Unit Research Group at Western Hospital and at the Veterinary Laboratories Agency (Weybridge), Darbre measured parabens in twenty human breast tumour tissues. The results, reported in 2004, demonstrated for the first time that parabens can enter as intact esters into the human body [3]. These findings were controversial at the time, but have since been substantiated by other scientists measuring parabens in human urine, blood, milk and seminal fluid.

To expand on this small study Darbre led a larger study in 2012, in collaboration with colleagues at The Genesis Breast Cancer Prevention Center (University Hospital of South Manchester) and SGS M-Scan analytical company, which measured intact paraben esters in a larger number of recent breast tissue samples, collected from four serial locations in the breast. Darbre and her colleagues reported intact parabens in 158 out of 160 human breast tissue samples [4]. As well, one of the parabens measured, *n*-propylparaben, was found in significantly higher concentrations in the region closest to the armpit. Though Darbre and her colleagues were cautious in their interpretation of this result, it did coincide with the disproportionate incidence of breast cancer in the upper outer quadrant of the breast, which Darbre herself had established to be more than 50% within the UK.

Establishing that parabens are present in breast tissue at functional concentrations:
Darbre then set out to establish whether the concentrations of parabens she had measured in the breast tissue samples were sufficient to stimulate proliferation of human breast cancer cells. In 2013, she reported for the first time that parabens can induce a transformed phenotype in human breast epithelial cells in suspension culture, a parameter closely associated with tumour growth in living organisms [5]. Darbre also showed that though individual parabens could be found in concentrations that had no observed effect on the proliferation of cancer cells, when combined at these low concentrations, they could stimulate cell proliferation [6]. This finding highlighted the importance of considering the consequences of combined parabens, not just individual compounds.

Although more research is required to determine whether the presence of parabens in the human breast is related to breast cancer development, the demonstration of the adverse properties of cosmetic chemicals like parabens together with measurement of their levels in human breast tissue are the first step to investigating whether there might be an impact on the development of breast cancer and are grounds for adopting a precautionary principle to improve safety regulations for use of parabens in cosmetics.

3. References to the research The research that led to the impact has been published in peer review journals and is rated as of at least 2* quality.

Outputs:

[1] Darbre P (2001) Hypothesis: Underarm cosmetics are a cause of breast cancer. *Eur J Cancer Prev* 10: 389-393. (Can be supplied upon request)

[2] Byford JR, Shaw LE, Drew MGB, Pope GS, Sauer MJ, Darbre PD (2002) Oestrogenic activity of parabens in MCF7 human breast cancer cells. *J Steroid Biochem Molec Biol* 80: 49-60. DOI: 10.1016/S0960-0760(01)00174-1

[3] Darbre PD, Aljarrah A, Miller WR, Coldham NG, Sauer MJ, Pope GS (2004) Concentrations of parabens in human breast tumours. *J Appl Toxicol* 24: 5-13. DOI: 10.1002/jat.958.
Note: This paper had a linked editorial (*J Appl Toxicol* 24: 1-4) and was ISI Top Fast Breaking Paper in Pharmacology and Toxicology for February 2005. As of July 18, 2013, this article has been cited by 293 papers (Google Scholar).

[4] Barr L, Metaxis G, Harbach CAJ, Savoy LA, Darbre PD (2012) Measurement of paraben concentrations in human breast tissue at serial locations across the breast from axilla to sternum. *J Appl Toxicol* 32: 219-232. DOI: 10.1002/jat.1786.
Note: This paper had a linked editorial (*J Appl Toxicol* 32: 305-309).

[5] Khanna S, Darbre PD (2013) Parabens enable suspension growth of MCF-10A immortalized, non-transformed human breast epithelial cells. *J Appl Toxicol* 33: 378-382. DOI:10.1002/jat.2753

[6] Charles AK, Darbre PD (2013) Combinations of parabens at concentrations measured in human breast tissue can increase proliferation of MCF-7 human breast cancer cells. *J Appl*

Toxicol 33: 390-398. DOI: 10.1002/jat.2850

4. Details of the impact

Adoption by industry:

Neal's Yard Remedies is an independent British manufacturer and retailer of natural and organic skin and body care products with stores in the UK, mainland Europe, North America, Asia, Australia, and the Middle East. In November 2012, Neal's Yard Remedies incorporated Darbre's research into their marketing tools and public messaging, including a video featuring Darbre and her research. They stated that "by avoiding parabens, we believe we have avoided subjecting our customers to a potentially dangerous and carcinogenic cosmetic ingredient. This is a perfect example of the precautionary principle" [a].

In June 2012, The Organic Pharmacy, a British manufacturer and retailer of organic health products with stores in the US, Europe, and Asia Pacific, incorporated Darbre's research into the information they make available to their customers. Darbre was an invited expert at their 'Prevent Cancer Evening', which was recorded and posted on their website [b]. In keeping with The Organic Pharmacy's ethos that "consumers have the right to make an informed choice" [b], the event aimed to provide guests with an opportunity to learn more about the cutting edge science being conducted on carcinogenic chemical compounds and has become part of the educational material the business provides to its customers.

Informing policy recommendations:

The Scientific Committee on Consumer Products (SCCP) provides the European Union Commission with the scientific advice needed to prepare policy and proposals relating to consumer safety, public health and the environment. They have prepared a series of opinions on parabens [e.g. [c], which cites Darbre *et al.* (2002) *J Appl Toxicol* 22(4):219-26] and in 2005 were specifically asked to prepare an opinion based on Darbre's findings linking underarm cosmetics and breast cancer [d, cites 10 articles by Darbre including [2]]. Though the final opinion of the SCCP was that there was insufficient evidence to suggest causation, the issue had successfully been raised with the European Commission.

In 2009, The Danish Ministry of the Environment conducted a survey and assessment of the risk to children less than three years old exposed to chemical substances in consumer products [e]. This assessment cited Darbre's research showing that parabens could accumulate in the skin and be absorbed [e, pg 179-180]. The survey, which included the research of Darbre and others, led to Denmark's Environmental Ministry taking a precautionary approach with young children and banning parabens in lotions and other cosmetic products aimed specifically at children under 3 years of age on March 15th, 2011 [f].

The ban by the Government of Denmark then prompted the European Commission to seek guidance from the Scientific Committee on Consumer Safety (SCCS) to determine whether the EU should take the same precautionary measures as Denmark [g]. Again, Darbre's research was used to inform the opinion of the Scientific Committee [f, cites [2] and two other articles by Darbre], which eventually came to the conclusion that there wasn't sufficient evidence to warrant the same action across the EU.

Supporting campaigns by non-government organisations:

Darbre's research has been incorporated into the public awareness campaign materials of numerous not-for-profit, non-government organisations around the world. These include, for example, one of Canada's leading environmental organisations, David Suzuki Foundation [g] and the Organic Consumers Association, representing 850,000 members in the US [h].

Increasing public awareness:

Darbre's research has raised awareness of the oestrogenic effects of parabens to the general public through extensive coverage in the media. Examples of this coverage include:

- BBC Radio 4's *Today* programme (12 Jan 2004) – 7.18 million listeners/week (2011 audience figure)
- Front page spread on *The Sunday Times* (11 Jan 2004) – readership* of 2,525,000/week
- Pg 4 of *The Observer* (11 Jan 2004) – readership* of 1,056,000/week

- *MailOnline* (12 Jan 2012) – 5.3 million visitors/day**
- *USA Today* (13 Jan 2012) – 26.3 million unique visitors/month**
- *Reader's Digest Australia* [http://www.readersdigest.com.au/information-about-parabens] – 373,956 unique visitors/month**
- *Sydney Morning Herald* (18 Mar 2013) – 2.5 million unique visitors/month**
- *New Scientist* (12 Jan 2004) – 9.7 million page views/month**
- *The Huffington Post* (12 Jan 2012) – 39 million unique visitors/month**
- Documentaries were made with Dr Darbre by BBC3 ("How dirty can I get?", 10 Sept 2007) and Channel 4 ("How toxic are you?", 11 Oct 2007 and "How toxic are your kids?", 18 Oct 2007) and by France2 Envoye Spéciale (3 Mar 2005).

*readership values from mediauk.com as of July 2013; **statistics from the company's website

Darbre's research is also helping to raise awareness through the materials produced by government agencies, such as the US Food and Drug Administration [i, cites 3], as well as charities, such as Cancer Active [j] and Breast Cancer Fund [k]. Darbre is currently a patron of CancerActive.

Finally, Darbre's research has also featured in numerous popular books including *Altering Eden: The Feminization of Nature* by award-winning BBC TV science producer D. Cadbury (1999), *Choosing to Heal: Surviving the Breast Cancer System* by J. Edwards (2007) and *Toxic Beauty: The Hidden Chemicals in Cosmetics and How They Can Harm Us* by D. Mellowship (2009).

5. Sources to corroborate the impact

[a] Neal's Yard Remedies (2012) *Philippa Darbre – The Problem of Parabens,* NYR Natural News Video Channel [video published on Nov 5, 2012]. <http://www.nyrnaturalnews.com/our-videos/?tubepress_video=megyJo2X_c8&tubepress_page=1>

[b] The Organic Pharmacy (2012) *Prevent Cancer Evening, hosted by The Organic Pharmacy,* Our Blog [website accessed online 19 Jul 2013]. <http://blog.theorganicpharmacy.com/?p=1879>

[c] SCCP (2005) *Extended Opinion on the Safety Evaluation of Parabens*, European Commission, Health & Consumer Protection Directorate-General, SCCP/0873/05. <http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_019.pdf>

[d] SCCP (2005). *Extended Opinion on parabens, underarm cosmetics and breast cancer,*European Commission, Health & Consumer Protection Directorate-General, SCCP/0874/05. < http://ec.europa.eu/health/archive/ph_risk/committees/04_sccp/docs/sccp_o_00d.pdf>

[e] Tønning K, Jacobsen E, Pedersen E, Strange M, Brunn Poulsen P, Møller L, Buchardt Boyd H (2009) *Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products*, Survey of Chemical Substances in Consumer Products, No. 102 2009, Danish Ministry of the Environment: Denmark. <http://www2.mst.dk/udgiv/publications/2009/978-87-92548-81-8/pdf/978-87-92548-82-5.pdf>

[f] SCCS (2011) *Clarification on Opinion SCCS/1348/10 in the light of the Danish clause of safeguard banning the use of parabens in cosmetic products intended for children under three years of age,* European Commission, Directorate-General for Health & Consumers, SCCS/1446/11.<http://tinyurl.com/na9kyra>

[g] David Suzuki Foundation (2013) 'Parabens', Issues, Health [website accessed online 19 July 2013] <http://tinyurl.com/pq4qcat>

[h] Organic Consumers Association (2004) 'Beware of Paraben Preservatives in Body Care Products [website accessed online 19 July 2013] <http://www.organicconsumers.org/bodycare/paraben011304.cfm>

[i] US Food and Drug Administration (2007) 'Parabens', Cosmetics, Product and Ingredient Safety [website accessed 19 July 2013] <http://tinyurl.com/4tujx7n>

[j] Cancer Active (2004) 'Stay smelling fresh', Cancer Watch Newsletter – February 2004 [website accessed online 19 July 2013] < http://www.canceractive.com/cancer-active-page-link.aspx?n=427>

[k] Breast Cancer Fund (2013) 'Parabens', Clear Science, Chemicals Glossary [website accessed online 19 July 2013] <http://tinyurl.com/n27bpko>