



ANNEX C - RESPONSE TEMPLATE

To: Stephen.fawbert@mhra.gsi.gov.uk

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From:

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Date: 14 August 2009

MLX 358 RESPONSE

Please tick box as appropriate

- We have no comments to make on the proposals in MLX 358
- Our comments on the proposals in MLX 358 are attached

ALL RESPONDENTS MUST TICK ONE OF THE FOLLOWING TWO BOXES

- My reply may be made freely available
- I wish my reply or parts of my reply to remain confidential*

*Please use the space below to explain why you feel the information in your reply should be treated as confidential. In line with the Freedom of Information Act 2000, if we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances.

Signed: _____ Date: **14 August 2009**

Teresa Leonardo Alves

1. Do you agree with the key elements of the European Commission proposal outlined in paragraph 13?

No, in order for the European Commission to fulfil its mission of protecting public health (article 152 of the Treaty establishing the European Community) the proposal for a directive on Information to Patients should be withdrawn. The European Health Ministers denounced the misguided approach contained in the proposal during the Employment, Social Policy, Health and Consumer Affairs (EPSCO) Council meeting (8-9 June 2009).¹ In so doing, the Council echoed the call of a vast majority of stakeholders vehemently opposed to direct-to-consumers communication by pharmaceutical companies.

HAI Europe stresses the importance of article 88 and 86 of Directive 2001/83/EC, which is the only legislative safeguard against the introduction of direct-to-consumer advertising of prescription medicines. Article 88 and article 86 should remain intact. There is no public health rationale for weakening or amending this regulation. However, the Commission's proposal for a legal framework foresees an increased role for the pharmaceutical industry in providing information to patients. This will introduce an opportunity for companies to supply information of a promotional nature directly to consumers, and to all intents and purposes, it will contribute to a relaxation of the current law, which precludes any direct or indirect advertising of prescription medicines to the public in Europe (Article 86.2 and Article 88).

In a highly competitive environment, drug companies must promote their own products above other preventive or curative options, thus any "information" they provide will be, by definition, of a promotional nature². As this "information" cannot be reliable or comparative, the whole proposal offers no added value for European citizens. The only real rationale for the Commission's proposal to change the current EU legislation seems to be to benefit the commercial interests of pharmaceutical companies by expanding their market reach. This is a useless exercise for both Europeans and Member States, representing additional bureaucracy and increased costs. Moreover, EU Member States have endorsed the *WHO Ethical Criteria for Medicinal Drug Promotion*, which specify that promotion "should not be designed so as to disguise its real nature."³

2. Do you agree with the UK government position at paragraph 16-18?

No, HAI Europe strongly argues that the pharmaceutical industry should not be granted an increased role in the provision of information on disease epidemiology, prognosis, or medical treatments to the public beyond what is currently contemplated in the European legislation.

The current initiative, rather than addressing the problem with a regulatory solution that prevents the provision of biased information through disguised advertising, seems instead to promote more misleading disguised advertising.

Evidence from other countries: The situation in Canada is of particular relevance to the current consultation, in that Canada prohibits direct-to-consumer advertising of prescription medicines, but has introduced limits to the enforcement of the law in response to strong pressure from the

pharmaceutical and advertising industries. One of the key initiatives that limits enforcement was an administrative policy that attempted to define non-promotional ‘information’ from pharmaceutical manufacturers. This has led to a plethora both of direct and disguised advertising. Although the volume of drug promotion is not nearly as high as in the United States, with full direct-to-consumer advertising of prescription drugs, many promotional messages reach the public with negative public health impacts. This is despite pre-screening by ‘co-regulatory bodies’ (Advertising Standards Canada and the Pharmaceutical Advertising Advisory Board). Examples include unbranded off-label promotion for orlistat (Xenical by Hoffman-LaRoche) for women wanting to lose weight; unbranded advertising messages using fear of death to sell a cholesterol-lowering drug (Lipitor by Pfizer); and television advertisements for several drugs that have been subject to Health Canada safety advisories, including cyproterone/estradiol (Diane-35) and more recently celecoxib (Celebrex). The messages in these advertisements often directly contradict the safety advisories recommending limited and judicious use.

Patient information should help users to analyse their concerns; to realistically assess their medical status; to understand when further investigations are necessary; to know what treatments exist along with their respective benefits and drawbacks; and to choose (or participate in the choice) from among the different available options. In order to make genuinely informed choices, above all, **patients need reliable comparative data.** But this crucial criterion has been arbitrarily excluded from the “quality criteria” proposed by the European Commission: «Comparisons between medicinal products should not be allowed».⁴

Pharmaceutical companies have a very specific part to play in promoting rational use of medicines, one which is strictly limited to improving the quality and clarity of the package labelling and patient information leaflets in compliance with the law (article 59). Evidence suggests that the pharmaceutical industry already have difficulty in implementing this minimum requirement. Attention should be paid to this failure of implementation by the UK authorities.

The priority should be for the MHRA to ensure that all information it receives on drug safety and effectiveness is publicly available, including all pre-market laboratory and clinical data and post-marketing studies. Additionally, regulatory agencies in all EU Member States should be strongly encouraged to implement their transparency obligations. The Commission could support the national regulatory agencies by providing a centralised web portal with access to all Patient Information Leaflets and European Public Assessment Reports. Much of the purported gap in patients’ and consumers’ information would be reduced if statutory obligations were met.

- 3. It would be very helpful if you could quantify any assessment of the impact of these proposals and the Commission options 2-4, as well as providing information about the type, and size of organisation that will be affected most. It would be helpful if your assessment were to include, but not be restricted to, the financial impact of these proposals.**

The lessons learned both from the United States and New Zealand, where direct-to-consumer-



advertising is allowed, and from direct-to-physician advertising practices in Europe indicate that excessive promotion of new medicines **leads to an increased demand for specific products that consumers do not necessarily need**⁵.

“Awareness” raising and “prevention”, “interaction [with health professionals]” and “compliance” can all be achieved through the promotion of independent public health campaigns on specific conditions, driven by the authorities and thus, avoiding “disease mongering”.⁶

Advertisements in general and direct-to-consumers advertising (DTCA) in particular, have been shown to drive choice of specific, expensive brand-name medicines rather than information.⁷

Over the past decade in the United States and New Zealand, DTCA of prescription drugs has increased sales for "blockbuster" drugs, such as rofecoxib (Vioxx), while providing a good return on investment (on average, \$3.66 per dollar spent). Not surprisingly, Gagnon and Lexchin have demonstrated that the US pharmaceutical industry invests twice as much on marketing and promotion than on research and development of new medicines.⁸

A large proportion of recently approved medicines provide no therapeutic advantage over existing alternatives; serious side effects are often identified a few years after market authorisation.⁹

More than \$1 billion USD were spent in the United States on DTCA for esomeprazole; yet the same therapeutic effects can be achieved with omeprazole. Benoxaprofen (Oraflex) and rofecoxib (Vioxx), withdrawn in 1983 and 2004 respectively, are testament to the ability of publicity campaigns to rapidly stimulate sales of new drugs with serious risks.

Rofecoxib led to an estimated 88,000 to 140,000 heart attacks in the United States, 44% of which were fatal. It was among the most heavily advertised drugs even in the four years after the first large-scale clinical trial showed evidence of cardiac risks. In a Kaiser Permanente study, 20% of first-time users of cyclooxygenase-2 inhibitors had requested prescriptions after seeing ads. They were 4 times less likely to adhere to treatment guidelines than other users.¹⁰ The US and New Zealand experiences also provide ample evidence of the difficulty in imposing restrictions to DTCA once it has become an established practice.

The monitoring of information, as defined in the legislative proposal, would entail significant human and financial resources. The MHRA should strive to uphold the current European legislative ban on DTCA while enforcing its implementation by monitoring industry practices, websites and media releases.

4. Do you think there are any additional measures that UK should lobby to be included in the proposals?

The following measures should be advocated by the UK, as they would consistently improve access to relevant and independent information around Europe and do not require changes to the current legislation:

- To make the officially approved leaflet more useful and accessible for patients (improve the readability and structure of the information conveyed, as well as the provision of adverse effects' information and recent pharmacovigilance decisions) by ensuring that pharmaceutical companies consistently abide by their **obligations relative to drug packaging and patient leaflets** (i.e. consultations with target patient groups) (enforcement of article 59 of Directive 2001/83/EC modified by Directive 2004/27/CE);
- To optimise **communication between patients and health professionals**: informing patients and fulfilling their needs implies a relationship of trust and interpersonal dialogue, which are the core responsibilities of healthcare professions;
- To encourage **national agencies to become proactive and more transparent providers of information** so as to guarantee full public access to data on the efficacy and safety of medicines and other healthcare products both before and after a product is marketed;
- To **develop and reinforce existing sources of comparative, unbiased information on treatment choices**;
- To put a **rapid and permanent end to the confusion of roles between the pharmaceutical companies and other actors** in the healthcare sector: full implementation and enforcement of the European regulation on pharmaceutical promotion, including measures to ensure that article 88 of Directive 2001/83/EC, is not weakened or undermined.

5. **Do you have any concerns that any of these measures could adversely impact on public health? Please explain your concerns.**

The European regulatory framework is clear (articles 86(2) and 88 of Directive 2001/83/EC modified by Directive 2004/27/EC):

Pharmaceutical companies are already permitted to provide information to the public on diseases¹¹ and to answer specific and individual questions (*article 86 transferred in the proposed article 100 b (a)*).

Disseminating the officially approved documents (art. 100b a) on prescription-only pharmaceuticals, namely the SPC and package leaflet on pharmaceutical companies' websites is already possible

under current EU legislation (i.e. France, the Netherlands, etc.). Hence, there is no real need for changes to allow their publication on marketing authorisation holders' websites. Marketing authorisation holders can simply place a link from their own websites to those of the regulatory agencies, where the information would be available.

To allow the pharmaceutical industry to draw up documents using only some of the elements of the SPC (Summary of Product Characteristics), disconnected from the others elements needed to understand them properly, and to produce another leaflet is nonsensical (*proposed article 100 b (b)*): it is inefficient and potentially confusing to have two types of leaflets circulating, one officially approved and a rewritten version produced by the manufacturer. The risk is that it will lead to the public dissemination of promotional information on prescription only medicines.

► **If the aim is to harmonise practices in Members States, actions at the national level would be the best way to ensure consistent interpretation/enforcement of articles 59¹² and 86.**

Impracticable regulations do not protect against infringements. The Commission proposes that "*monitoring should take place after dissemination of information, with certain exemptions*". Measures intended to control direct-to-consumer advertising in the United States and direct-to-prescriber advertising in Europe have clearly failed. The relevant 'regulatory bodies' tend to detect infringements too late, often when the damage has already been done, and have difficulties imposing penalties¹³. Bearing in mind that the US Food and Drug Agency has expanded its budget to improve the monitoring of direct-to-consumer-advertising by pharmaceutical companies, **the Commission's proposals to regulate "information to patients" seem to fall short.**

► **No previous (ex ante) controls are planned and sanctions are to be imposed retrospectively**, once the "information" has been disseminated and the public harm has taken place.

The plan to allow companies to "give information about scientific studies" authorises a dangerous marketing practice. It stimulates demand, thus favouring the commercial launch of drugs being trialled for new indications on the basis of partial results, with insufficient time to evaluate the drug's efficacy and safety for such new indications. In a fiercely competitive climate, pharmaceutical companies are under pressure to champion the drugs they market to the detriment of other preventive or curative means, making the "information" they provide promotional by nature. Their conflicts of interest are an insurmountable obstacle to objectivity.

Some examples:

- Schering Plough and Merck spent US \$200 million in 2007 advertising Vytarin (ezetimibe + simvastatin) to the US public. Simvastatin is off-patent and available generically at a much lower price. There is no evidence that ezetimibe reduces the risk of heart attack or stroke; the only clinical trial evidence available until April 2006 was limited to lowering of cholesterol, by blocking absorption. In April 2006, the first clinical trial was completed on effects on arterial



plaque. Ezetimibe did not affect the build-up of arterial plaque. Publication of this trial did not occur until April 2008. The manufacturers would have been aware of trial results when they spent US \$200 million spent on advertising in the US in 2007. The US public had no access to this information.

- Similarly, Merck spent US \$550 million advertising Vioxx (rofecoxib) to the US public, mainly after the results of the VIGOR trial had shown an increase in cardiovascular events and total serious adverse events.

The proposals to permit pharmaceutical companies to broaden the scope of the campaigns they are allowed to produce “in the interests of public health” (proposed article modifying article 88(4)), and to communicate on non-interventional studies (proposed article. 100 b (d)) are two indications that the aims of these proposals are to allow direct-to-consumer promotion of prescription medicines and to build loyalty to brand products: even the Commission has recognised that non-interventional studies are “often of poor quality and frequently promotional”.¹⁴

In addition, the already existing provision for “Factual informative announcements” on prescription medicines by the industry (article 86 transferred in the proposed article 100 b (c)) is of little value for patients’ treatment regimes. However, they are of enormous value as reminder adverts for their product, and are hugely effective at inflating sales through emotive branding images and messages.¹⁵

Instrumentalisation of health professionals.

The Commission’s proposes that “*material provided by the marketing authorisation holder to healthcare professionals for distribution to patients*” will not be covered by the title VIIIa (Information and advertising) (*proposed article 100a point 2 (b)*). This means that “materials” prepared by the pharmaceutical companies would not be subject to any control (no “quality criteria”, nor monitoring to comply with). This is tantamount to advertising. The EU Commission will be reducing health professionals to mere “brochure distributors” on behalf of pharmaceutical companies. The inclusion, in any “information” provided by pharmaceutical companies, of “*a mail address or email address allowing the general public to send comments to the marketing authorisation holder*” (*proposed article. 100 d point 2 (d)*) shows how such “information” is likely to be used for promotion, enabling pharmaceutical companies to contact patients directly, bypassing health professionals.

- ▶ **“Direct-to-consumer advertising” (DTCA), under the guise of “direct-to-consumer - information” aims to increase sales by contacting directly the public directly and bypassing health professionals.**

REFERENCES AND EDITOR’S NOTES

¹ Press release “2947th Council meeting – EPSCO” 8-9 June 2009
http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lisa/108380.pdf



² The Directorate for Competition's "Pharmaceutical sector enquiry report" how far pharmaceutical industry are going to delay competition. The proposals on "information to patients" are yet another tactic to delay generic competition by building "brand loyalty" to their own medicines.

³ WHO Ethical Criteria for Medicinal Drug Promotion, accessible at <http://www.who.int/medicinedocs/collect/edmweb/pdf/whozip08e/whozip08e.pdf>

⁴ European Commission Public consultation, Legal proposal on Information to Patients, page 7

⁵ Kravitz et al. "Influence of patients requests for direct-to-consumer advertised antidepressants: a randomized controlled trial" JAMA 2005; 293: 1995-2002; Mintzes B et al. "How does direct-to-consumer advertising (DTCA) affect prescribing? A survey in primary care environments with and without legal DTCA" CMAJ 2003; 169 (5): 405-412.

⁶ Disease mongering is a well documented marketing practice which consists expanding disease definitions and providing inaccuracies about disease prevalence, risks, potential treatment benefits, all in order to increase sales.

⁷ Bull World Health Organ (2009) Direct to Consumer advertising under fire, by Humphreys, G.; 87:576-577.

⁸ GAGNON, M.-A. & LEXCHIN, J. (2008) The Cost of Pushing Pills: A New Estimate of Pharmaceutical Promotion Expenditures in the United States. PLoS Med, 5, e1.

⁹ Kravitz et al. "Influence of patients requests for direct-to-consumer advertised antidepressants: a randomized controlled trial" JAMA 2005; 293: 1995-2002; Mintzes B et al. "How does direct-to-consumer advertising (DTCA) affect prescribing? A survey in primary care environments with and without legal DTCA" CMAJ 2003; 169 (5): 405-412.

¹⁰ MINTZES, B. (2009) Should Canada allow direct-to-consumer advertising of prescription drugs?: NO. Can Fam Physician, 55, 131-133.

¹¹ They make the most of the opportunities provided by this framework, often going beyond with disease "awareness" campaigns and even disease mongering.

¹² Article 59 of Directive 2001/83/EC modified by Directive 2004/27/EC lays down the specific role for the pharmaceutical companies in improving the quality and clarity of labelling and the package leaflet.

¹³ General Accounting Office (GAO) "Prescription drugs: improvements needed in FDA's oversight of direct-to-consumer advertising". November 2006. www.gao.gov/new.items/d0754.pdf: 52 pages.

¹⁴ "EU pharmacovigilance: public consultation on legislative proposals" (point 3.2.5). Dec 2007. ec.europa.eu/enterprise.

¹⁵ Mintzes B "La publicité directe au public pour les médicaments: une pilule pour chaque maladie ou une maladie pour chaque pilule?" Rev Prescrire 2006: <http://www.prescrire.org/editoriaux/EDI26685.pdf>.