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INFLUENCE Compliance programmes: not to be confused with risk management plans

● The European Medicines Agency (EMEA) has confirmed to us in writing that no drug companies have yet been asked to contact patients directly, through so-called compliance programmes, as part of a marketing authorisation agreement.

In late 2006, fears were raised in France that company-sponsored compliance programmes would soon be approved (1). A storm of objections by concerned parties forced the health minister to back down, at least temporarily, in early 2007, but not without first attempting to push the bill through parliament (2-4). Curiously, during the parliamentary debate, the minister claimed that company-sponsored compliance programmes were required as part of European marketing authorisation (2).

We asked the European Medicines Agency (EMEA) whether or not this was true (5).

EMEA responds. The answer we received from the EMEA on 27 April 2007 refers to the legislative framework and makes things perfectly clear (6).

According to Directive 2001/83/EC on human medicines, as modified by Directive 2004/27/EC, applicants for market authorisation must describe how they intend to ensure pharmacovigilance for their products, if necessary, through a risk management plan (6). In some cases, these plans include 'risk-minimisation activities', that generally consist, according to the EMEA, of simply adding warnings to the summary of product characteristics and the patient information leaflet, and, sometimes, making educational materials available (6).

EMEA does not ask companies to establish compliance programmes. The EMEA explained that the European Committee for Medicinal Products for Human Use (CHMP) sometimes asks for post-market studies intended to show how the drug is actually used, and that "*in some rare cases*" this may include studies of compliance (6). However, the EMEA stressed that these studies are purely observational and never interventional. The EMEA was "*not aware of any centrally authorised medicine where compulsory compliance with a particular treatment has been part of the risk management programme*" (6).

The EMEA's statement is borne out by the risk management plans posted on the EMEA website, as part of European public assessment reports (EPARs). Additional requirements, sometimes requested by the French Health Products Safety Agency (AFSSAPS), and now published on its website, do not involve either direct or indirect contact between drug companies and patients. And, whenever educational materials are intended for patients, they must be given to the patient by a healthcare professional, not directly by the company (**a**).

Therefore, it is wrong to claim that the French or European drug regulatory agencies require drug companies to provide direct assistance to patients with their treatment.

Playing with words. Nevertheless, in July 2007, the French pharmaceutical industry federation LEEM, in its "key messages" on "patient assistance programmes" stated (our translation) that: "*the drug regulatory agencies (EMEA and AFSSAPS) create, in addition, through risk management plans, a requirement for drug companies to better inform patients and to better manage their treatments*" (7). The same document also states that *compliance* to treatment is one objective of assistance programmes (7).

Even if LEEM points out that, when implementing these programmes, "*a firm never has direct contact with patients*", there is a risk that pressure will be exerted through service providers.

Patients and healthcare professionals must remain vigilant, for example by watching out for toll-free telephone numbers included in educational materials (or even on drug packaging and leaflets) and for service providers that contact patients on the drug companies' behalf.

Watch this space.

a- For example, among the most recent risk management plans, the plan for Symbicort° (budesonide + formoterol) states that the asthma follow-up notebook provided for in the plan "will be given to patients by the prescribing physician" (ref 8). The plan for Acomplia° (rimonabant) is somewhat vague; in its French version, AFSSAPS added: "provision, by the firm, of documents on proper usage and information on risks intended for healthcare professionals and patients" (ref 9). But the EMEA document states that the 'customer care programme' must be designed so as to "provide healthcare professionals with educational support tools that can assist their patients" (ref 10).

Selected references from Prescrire's literature search.

1- Prescrire Rédaction "Programmes des firmes pharmaceutiques d'"aide à l'observance": l'imposture" *Rev Prescrire* 2006; **26** (271): 300.
2- Medicines in Europe Forum "Projet de loi sur les médicaments: un débat tronqué" 18 January 2007. www.prescrire.org: 2 pages.
3- Medicines in Europe Forum "Programmes d'"observance" des firmes: la société civile enfin entendue" 25 January 2007. www.prescrire.org: 1 page.
4- Prescrire Rédaction "Programmes industriels d'"aide à l'observance": répit de courte durée" *Rev Prescrire* 2007; **27** (285): 542.
5- Prescrire Editorial Staff ""Risk management plans – hardly reassuring!" *Prescrire Int* 2007; **16** (91): 216-217.
6- EMEA "EMEA compliance programme information - Courrier à la revue Prescrire" 27 April 2007: 2 pages.
7- LEEM "Programmes d'accompagnement des malades. Les messages clé du LEEM" 6 July 2007: 2 pages.
8- Afssaps "Plan de gestion de risque des spécialités pharmaceutiques Symbicort° - AstraZeneca" July 2007: 2 pages.
9- Afssaps "Plan de gestion des risques de la spécialité pharmaceutique Acomplia° - Sanofi-Aventis" 8 August 2007: 2 pages.
10- EMEA-CHMP "EPAR-Acomplia (revision 4) - scientific discussion": 41 pages; posted on the EMEA website on 31 May 2007.