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## Paediatric drugs - Who benefits from the European Paediatric Regulation?



The stated aim of the Paediatric Regulation (European Regulation (EC) No 1901/2006, adopted in 2006) was to encourage the development of drugs suitable for children (1). However, this Regulation was constructed with insufficient emphasis on children's needs.

It is true that the Paediatric Committee that was created within the European Medicines Agency (EMA) has been tasked with identifying children's unmet needs. But it is too often satisfied with producing inventories of drugs authorised for use in adults that are prescribed off-label for children in the various Member States, even though some of these practices are harmful to children (2).

The Paediatric Regulation focuses primarily on providing incentives for pharmaceutical companies that introduce paediatric forms of drugs already marketed for adults, or that market new drugs for paediatric use, even if these new drugs do not represent a therapeutic advance for children (2).

In September 2012, five years after the Regulation came into effect, the European Commission organised a public consultation to learn lessons from the experience acquired since its implementation (3).

*Prescrire* chose to respond to this consultation by detailing one example in France that illustrates particularly well

some of the most lamentable aspects of the implementation of the Paediatric Regulation: the paediatric form of *losartan* (Cozaar<sup>o</sup>), an oral suspension for the treatment of hypertension in children (4).

The poorly-designed packaging for Cozaar<sup>o</sup> oral suspension is unsuitable and dangerous for children. This drug is difficult to obtain and is not reimbursable; furthermore, *losartan* is not the standard treatment for children with hypertension. Yet, in accordance with the Paediatric Regulation, the company that markets Cozaar<sup>o</sup> oral suspension was granted a 6-month extension to its market exclusivity in France on all forms of Cozaar<sup>o</sup>, even for its non-paediatric indications (4).

In its response, *Prescrire* also pointed out that the other component of the Paediatric Regulation, the paediatric-use marketing authorisation (PUMA), had not yet led to the development of any drugs that meet children's real needs (4).

*Prescrire* urged the EMA's Paediatric Committee to profoundly improve the implementation of the Paediatric Regulation, so that it better meets the needs of children, beginning with:

- Prioritising children's real therapeutic needs in the lists of "unmet paediatric needs", rather than simply producing inventories of existing practices without evaluating their appropriateness in children;
- Ensuring that drugs with paediatric indications represent a tangible therapeutic advance;
- Reducing the dangers to which children are exposed, by demanding improvements to the numerous packaging materials that are unsuited to paediatric use, starting with those that have already been implicated in medication errors and accidents (a)(1,4).

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a- The Paediatric Regulation laid down a procedure for the reassessment of paediatric data on old drugs by the Paediatric Committee (Article 45 of ref 1). In practice, this procedure is mainly used to harmonise the paediatric information in the various national summaries of product characteristics, e.g. to add paediatric dosages or a statement that no data are available in children, as appropriate. Each year, 40 to 50 drugs are reassessed through this procedure (ref 4). Health authorities should use these reassessments to request improvements in the packaging of drugs with paediatric indications, to make them more suitable for paediatric use (ref 4).

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### Prescrire's policy advocacy

In the field of health care, each policy decision has an influence on the conditions under which healthcare professionals practice and on patients' access to health care, factors which determine the quality and safety of patient care.

Changing the legislative framework for health products is a sensitive matter. It is certainly too sensitive to give free rein to vested interests or to adopt a short-sighted approach, which often put industry's short-term economic interests before public health.

That's why, for over 30 years, in addition to helping healthcare professionals and patients choose the most relevant treatment options, *Prescrire* has been working to improve health policy, first and foremost in the interest of patients. By analysing the strengths and weaknesses of the regulatory environment from the perspective of all parties that have a stake in health care: industry, health authorities, health insurance organisations, healthcare professionals, and patients. Together with other members of the International Society of Drug Bulletins (ISDB), *Prescrire* has been an active participant in international campaigns to increase the transparency and independence of drug regulatory agencies, public access to clinical trial data, etc.

*Prescrire* is an active member of the Medicines in Europe Forum (MiEF), which was founded in 2002, when the first drafts of the 2004 European legislative framework for medicinal products were proposed, to act as a counterbalance to the powerful pharmaceutical industry lobby.

We analyse draft laws and regulations in detail, anticipate and explain any potential dangers posed to patients or to the provision of health care and other social benefits, suggest alternatives, meet with members of parliament, highlight potential consequences to Member States' health ministers and European Commission departments (Directorates-General), and organise public debates. These sustained, rigorous campaigns often meet with success. For example, the tireless perseverance of *Prescrire* and other civil society organisations that have been campaigning over the past 10 years has prevented the European Commission from legalising direct-to-consumer advertising of prescription drugs in Europe.

These sustained campaigns, as well as other ad hoc actions, are an integral part of the socially responsible approach adopted by the health professionals who subscribe to and support *Prescrire*.

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**Selected references from Prescrire's literature search.**

1- "Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004" *Official Journal of the European Union* of 27 December 2006: L378/1-L378/19.

2- Prescrire Editorial Staff "Application of the European regulation on paediatric drugs: remain vigilant!" *Prescrire Int* 2008; **17** (93): 38-41.

3- European Commission - Health and Consumers Directorate-General "General report on experience acquired as a result of the application of the Paediatric Regulation (Article 50(2) of Regulation (EC) No 1901/2006). "Experience acquired" and "lessons learnt" submitted for public consultation - Deadline for public consultation 28 November 2012" 18 September 2012: 13 pages.

4- Prescrire Editorial Staff "Who benefits from the European Paediatric Regulation?"

Response to the European Commission's public consultation on the lessons learnt from the first 5 years of application of the Paediatric Regulation" Paris, 28 November 2012. [english.prescrire.org](http://english.prescrire.org) accessed 18 December 2012: 6 pages.

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## The powerful influence of pharmaceutical sales representatives

**I**t has long been established that visits by pharmaceutical sales representatives have a detrimental effect on the quality and cost of prescriptions (1,2). It is best not to underestimate their influence, while the pharmaceutical industry and French Ministry of Health continue to legitimise these visits through the "Sales Visit Charter", a code of conduct establishing norms for sales visits (3).

**A survey of 179 doctors in Brittany (France).** A study conducted in Brittany in 2009-2010 provides a concrete example of the influence that pharmaceutical representative visits have on doctors (4). Through telephone interviews, a profile was drawn up of 179 doctors selected at random from the 2950 general practitioners in Brittany. Information was collected on the frequency of meetings with pharmaceutical sales representatives, continuing education habits, type of medical practice and relationships with pharmaceutical companies. These doctors were then divided into 6 groups, based on the frequency of meetings with pharmaceutical sales representatives (4).

The Rennes regional state health insurance office (CRAM) then supplied aggregated data for the 6 groups, which were used to analyse their prescribing behaviour, including: the cost and number of prescriptions, and the drugs they tended to prescribe within certain pharmacotherapeutic groups (4).

**Measurable industry influence.** According to this study, the doctors who met most frequently with pharmaceutical sales representatives conducted shorter consultations with their patients and more consultations per day. They had been in practice longer, were more likely to read free medical journals and less likely to read medical journals requiring a subscription (4).

These doctors prescribed more angiotensin II receptor blockers, glitazones, gliptins (dipeptidyl peptidase-4 inhibitors) and certain antibiotics such as *moxifloxacin*, *levofloxacin* and *telithromycin* within their respective therapeutic classes (4). All of these drugs are promoted by pharmaceutical sales representatives at the expense of better evaluated, safer or cheaper alternatives.

This study also showed a statistically significant correlation between the fre-

quency of meetings with pharmaceutical sales representatives, and the number and cost of their prescriptions (4).

**Refuse to see pharmaceutical sales representatives in the interest of better patient care.** The harmful effects of presentations by pharmaceutical sales representatives sidetrack healthcare professionals from a fundamental goal, which is to offer patients the most appropriate treatments. This is yet another reason to follow the example of the 17% of general practitioners surveyed who refuse to see pharmaceutical sales representatives (4).

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**Selected references from Prescrire's literature search.**

1- Prescrire Editorial Staff "15 years of monitoring and one simple conclusion: don't expect sales representatives to help improve healthcare quality" *Prescrire Int* 2006; **15** (84): 154-159.

2- Spurling GK et al "Information from pharmaceutical companies and the quality, quantity, and cost of physicians' prescribing: a systematic review" *Plos Medicine* 2010; **7** (10): 22 pages.

3- "Visiteurs médicaux: le secteur ouvert à un réseau de médecins sentinelles" *Dépêche AFP*; 1 March 2013; 1 page.

4- Foisset E "Étude de l'impact de la visite médicale sur la qualité des prescriptions des médecins généralistes bretons" Medical thesis n°2912002, Brest, 2012: 181 pages.



### NEW PRODUCTS

- *Pasireotide* in Cushing's disease
- *Everolimus* in breast cancer
- *Axitinib* in kidney cancer

### ADVERSE EFFECTS

- *Piribedil*
- Thrombotic risk of contraceptive transdermal patches

### REVIEWS

- Antithrombotic drugs and ischaemic stroke
- Acupuncture and chronic joint pain

### Outlook

- Euthanasia in Belgium, the Netherlands and Luxembourg