

11- Prescrire Rédaction "DCI des amphétamines: dérivés par absence de segment-clé" *Rev Prescrire* 2013; **33** (362): 938-939.

12- Prescrire Rédaction "Prescrire en questions: le racécadotril est-il un opiacé?" *Rev Prescrire* 2009; **29** (308): 475-476.

13- WHO "Proposed International Nonproprietary Names: List 83. Amendments to previous lists" *WHO Drug Information* 2000; **14** (2): 132.

14- Prescrire Rédaction "Le segment-clé du mois: -parin (ux)" *Rev Prescrire* 2002; **22** (232): 662.

15- Prescrire Editorial Staff "Serotonin agonist or "hidden" neuroleptic?" *Prescrire Int* 2011; **20** (116): 119.

16- WHO Programme on International Nonproprietary Names (INN) "48th Consultation on International Nonproprietary Names for Pharmaceutical Substances - Geneva, 31 March-3 April 2009 - Executive summary" September 2009: 7 pages.

17- "Article 10 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001, amended, on the Community code relating to medicinal products for human use" *Official Journal of the European Union* L311 of 28 November 2001: 67.

18- Prescrire Rédaction "D'alfa à zêta, toutes les époétines se valent" *Rev Prescrire* 2009; **29** (304): 105.

19- Medicines and Healthcare products Regulatory Agency (MHRA) "Biosimilar products" *Drug Safety Update* 2008; **1** (7): 8.

20- "Commission Implementing Regulation (EU) No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council" *Official Journal of the European Union* L159 of 20 June 2012: 5-25.

21- Pharmaceutical Research and Manufacturers of America (PhRMA), Biotechnology Industry Organization (BIO) "Letter to FDA" 25 June 2012: 2 pages.

22- US FDA "FDA gives update on botulinum toxin safety warnings; established names of drugs changed" 3 August 2009; 2 pages.

23- US FDA - CDER "Application number 125-294. Proprietary name review" 2 August 2012: 58 pages.

24- US FDA - CDER "Application number 125-418. Proprietary name review" 27 July 2012: 44 pages.

25- EMA - CHMP "European Public Assessment Report - Vimpat. Scientific discussion" 29 August 2008: 52 pages.

26- Prescrire Rédaction "Lettre relative à la dénomination du lacosamide dans son dossier d'évaluation" 21 October 2008: 1 page.

27- EMA "Request on VIMPAT[®]" 21 January 2009: 1 page.



Translated from *Rev Prescrire* January 2014; **34** (363): 57

Premarketing trials: too few patients

How many clinical trial participants are exposed to a new drug before it is granted EU marketing authorisation? To answer this question, a Dutch and British team analysed European marketing authorisations granted between 2000 and 2010 (a)(1).

Too few patients, too little time.

The authors found that 161 new drugs authorised during this period (excluding orphan drugs) were each tested on an average of about 1700 subjects (1); 56% were tested in fewer than 2000 subjects and 12% in fewer than 500.

Drugs intended for long-term use were tested in an average of 2340 subjects, slightly more than other drugs, but only 30% of these drugs were tested for at least 12 months in more than 1000 patients (1).

The authors of this analysis concluded that too few patients were enrolled in premarketing trials to assess the long-term efficacy and potential harms of the drugs in question (1).

Regulatory agencies are complacent. There is no legal minimum placed on the number of participants to be included in clinical trials of new drugs prior to marketing authorisation. As a result, companies tend to include the smallest number of participants necessary to achieve the statistical power required to establish efficacy (1,2).

Regulatory agencies are too inclined to accept substandard evaluations: for example, those that are based only on surrogate endpoints or do not include comparative trials versus standard treatments. The small number of persons in whom new drugs are tested further highlights the low standards that regulatory agencies require drug companies to meet. The end result is that patients are exposed to a risk of poorly documented or totally unexpected adverse effects that arise during routine use (3).

Post-marketing surveillance is no substitute for thorough initial assessment, which is the only way to protect patients from the harmful effects of new drugs. Legislation governing clinical trials must be strengthened, not relaxed.

©Prescrire

a- The authors of this study worked in Dutch universities or in Dutch and British regulatory agencies (ref 1).

Selected references from Prescrire's literature search.

- 1- Duijnhoven RG et al. "Number of patients studied prior to approval of new medicines: a database analysis" *PLoS Med* 2013; **10** (3): e1001407.
- 2- Prescrire Rédaction "Puissance d'une étude comparative. À prendre en compte pour interpréter certains résultats" *Rev Prescrire* 2008; **28** (298): 634-636.
- 3- Prescrire Editorial Staff "The power of a study: detecting teratogenicity" *Prescrire Int* 2014; **23** (145): 25.