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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.

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

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