EDITORIAL

THE NUMBERS GAME

As a discipline, we are obsessed by numbers, whether it is the number of new drugs, or dollars spent or months taken for each phase of the pipeline. We quote them enough, but can we have confidence in the figures we use?

It is said that when asked what could be inferred about the Creator from the works of nature, the noted evolutionist J. B. S. Haldane replied that the Lord seemed to have "an inordinate fondness for beetles". Whatever else one has picked up from studying the first year's issues of *Nature Reviews Drug Discovery*, one thing we know for sure is that we in the field of drug discovery and development have an inordinate fondness for numbers.

We each have our favourite. It might be 'US $802 million', or '15 years' or '1 in 5,000'. These figures are so often quoted that you probably know what they stand for already. We use them to top-and-tail our talks, or our papers, and generally to frame our thoughts on the subject in terms that show what a complicated, lengthy and expensive business it is to develop a drug. For these purposes, it doesn't really matter whether the 802 million is in dollars or pounds, or whether it is 15 or 20 years. The point is that these are big numbers. But we also use them as benchmarks against which to qualify and quantify our success rate, and it is in this respect that the values that we set on these parameters might be said to count. We ought to be sure of our facts.

So, if these are our measures of progress, how confident are we that they are right? Well, the US $802 million price tag for developing a new drug, for example, comes from a most reputable source — the Tufts Center for the Study of Drug Development (CSDD). But this includes both the cost of failed drug candidates and missed opportunities; in other words, the imaginary costs of those projects that couldn't be pursued owing to the fact that resources were committed elsewhere. Hard things to quantify, to be sure. And 15 years as the average time from initial concept to marketed drug sounds reasonable, but not so useful a measure when you bear in mind that drugs for endocrine disorders spend almost twice as long in clinical testing as anti-infectives. As for attrition rates, the CSDD estimates that only 1 in 5,000 compounds tested in animals makes it through to market, but that again is necessarily indication specific. Although these figures are among our more dependable old chestnuts, a little qualification wouldn't go awry.

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Some other intriguing, and much discussed, numbers are even harder to pin down. How many marketed drugs are there, for example? If you ask the FDA, you will find that there are 19,000, but that includes different formulations, including 150 ibuprofens. Asking around indicates that dealing just with those drugs that have different molecular structures gives a worldwide total of around 2,500, but there is no single source for this information. As for the number of molecular targets against which drug therapies might be developed, anything between 600 (REF. 1) and 10,000 (REF. 2) seems an acceptable estimate. Perhaps the widest variation of all is found in estimates of the potential number of drug-like molecules that could theoretically be synthesized. Figures of between 1×10^{18} and 1×10^{100} molecules are regularly seen, although from a practical standpoint it has to be admitted that both numbers are equally mind-boggling.

One number that we've avoided mentioning so far, but an easily quantifiable one that is on everyone's mind, is the pitiful tally of new drug approvals so far this year. At the time of writing, just 14 new molecular entities have received FDA approval in 2002, far down on even the worryingly low total of 24 in 2001. At this productivity rate, and with only a small minority of these products destined to make blockbuster status, it is hard to see where the revenues to fund future expansion of R&D programmes are going to come from. But that's a whole different set of numbers. And as for beetles? 350,000 species at the last count, and growing.

1. Hopkins, A. L. & Groom, C. R. The druggable genome. *Nature Rev. Drug. Discov.* **1**, 727–730 (2002).
2. Drews, J. Drug discovery: a historical perspective. *Science* **287**, 1960–1964 (2000)