

Box 10.1: Toxicity studies in humans: number of trial participants required to be 95 % certain* of detecting cases of adverse events directly related to the medicine under study

Incidence	1 case	2 cases	3 cases
1 in 100	300	480	650
1 in 200	600	980	1,300
1 in 1,000	3,000	4,800	6,500
1 in 2,000	6,000	9,600	13,000
1 in 10,000	30,000	48,000	65,000

* A confidence limit of 95% ($P < 0.05$) is generally agreed to be an acceptable level of certainty for trial data. Thus, 300 people would be needed to ensure 95% confidence to identify one person who will experience adverse reactions for which the average incidence is 1 in 100. (100, or 200 trial participants would give far lower levels of certainty). Higher levels of certainty are possible, but require disproportionately higher numbers of trial participants. As the table shows, higher numbers are also required to identify adverse events that occur less frequently. The closer the number of trial participants is to the number of people who will eventually use the medicine being assessed, the higher the levels of certainty. Complete certainty is, for statistical and practical reasons, impossible to achieve. See also: Stark NJ (2000) *Clinical Trials Design, Third Edition*, Clinical Device Group Inc, Chicago, IL; Friedman LM, Furberg CD and DeMets DL (1999) *Fundamentals of Clinical Trials* (Springer); Kirby A, GebSKI V and Keech AC (2002), Determining the sample size in a clinical trial, available at: http://www.mja.com.au/public/issues/177_05_020902/kir10425_fm.html. Accessed on: 3 May 2005.