

# MOUSE TO MAN: STATISTICAL PROBLEMS IN BRINGING A DRUG TO CLINICAL TRIAL

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## 1. Introduction

Problems of inductive inference and the ethics of the clinical trial of new drugs have led statisticians to pay much attention to the stopping rules in experiment designs [1], [2], [3]. I suggest that for clinical trials the statisticians should probably be paying as much attention to the problem of starting rules. When should a new material go into clinical trial? At what dose? At what frequency? By what route?

“Starting” problems also reflect problems of inductive inference, but of a different order of magnitude, or of a different qualitative nature than the problems of inductive inference following clinical trials. There the question is how to extend the findings on a small group of humans, selected in some special way, treated under some special circumstances, by special physicians, to the much larger group of humans suffering from the same illness, but to be treated under less specialized circumstances by less specialized physicians in less specialized institutions. In the preclinical trial phase, the earliest work is done on non-human species, almost always with different metabolic schemes and systems than man. The jump from these results to man is sometimes a large leap, made mostly in the dark.

If inferences within a species are difficult, as almost all writers on clinical trials attest by their urging of cautious generalizations and limited extensions of the trial results [4], [5], then what must be the difficulties of making the species to species jump that the preclinical trial work requires? I see three major pretrial problems for which a body of statistical theory may need to be built. Two of the three derive from the species to species problem.

## 2. Predictability for man of screening in lower animals

The first problem is, why try a given new material in man? Either a strong biochemical rationale has been developed for the action of the material, or work in lower animals has shown activity against the illness in which we are interested. Signs of this activity are often found through a screening process, and the statisticians have attended to the development of efficient screening procedures