



## **THE DAY THE SKY FELL IN; TGN 1412 AND WHAT HAPPENED NEXT**

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In March, 2006, a phase 1 clinical trial of a monoclonal antibody, TGN 1412 which had been approved under the European Clinical Trials Directive and was being conducted at Northwick Park Hospital in London, went badly wrong. The six healthy volunteers who had been given the drug became acutely ill within 2 hours of dosing and by 16 hours all were in intensive care with lung damage, renal failure, disseminated intravascular coagulation and loss of consciousness. All survived after many weeks of illness.

TGN 1412 is a superagonist for CD28 receptors on T cells; binding studies had shown identical binding characteristics in man and the cynomolgus monkey. The initial dose given to man was 500 fold less than the no adverse effect level in the monkey.

Investigations by the UK medicines regulatory authority and independently by the UK government showed that the cause of the mishap was a massive release of cytokines.

This trial has raised many issues about the conduct of such studies and their regulatory approval and these will be discussed.