TOXICITY TESTING OF BIOTECHNOLOGY DRUGS-EUROPEAN AND ICH PERSPECTIVES.

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The toxicity testing of biotechnology drugs in Europe and North America has been performed using a rational, scientifically-based 'case-by-case' approach. Some of the key points to be considered in designing the toxicity programme include the biological responsiveness of the test species to be used, the clinical exposure pattern, the kinetics of the test material and the potential for immunogenicity of immunotoxicity. Many of these points have been taken into account in the drafting of the ICH Step 4 document on the Pre-Clinical Safety Testing of Biotechnology-derived drugs, released at the ICH4 meeting in Brussels in July 1997.

The main points in the ICH guideline will be briefly outlined, and then specific comments will be made concerning different classes of biotechnology drugs, including recombinant peptides, monoclonal antibodies, as well as DNA based therapeutics(anti-sense and gene therapy). Based on Huntingdon's experience with these types of products, guidance will be given on practical issues such as duration of toxicity studies, toxicokinetic studies and the approaches to monitoring for antibody formation. The importance of specific and fully validated bioanalytical methods will be stressed.

As for all good toxicity testing programmes, the studies performed on biotechnology drugs should provide information that is relevant to the human risk assessment in terms of potential target organ or other toxicities, starting doses for Phase I studies, and kinetics of the test material.