

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 361

DOCKET NO. 2004N-0432

Radioactive Drugs for Certain Research Uses: Public Meeting – 16th November 2004-10-12

Presenter: Professor R Colin Garner BPharm PhD DSc FRCPATH
Address: Innovation Way, Heslington, York YO10 5NY, United Kingdom
Phone No: +44 (0)1904 561561
Email: colin.garner@xceleron.co.uk
Affiliation: Xceleron Ltd

Abstract

The costs of drug development have increased substantially over the past few years whilst the numbers of new drugs registered by the FDA has fallen. The result is that (1) patients and their re-imburement agencies will have to pay more for their prescription drugs and (2) delays are occurring in providing potential life-saving drugs to patients. The FDA in March 2004 published a White Paper entitled 'Innovation, stagnation – challenge and opportunity on the critical path to new medical products'. In this document it is argued that new tools need to be used to accelerate the drug development process.

One enabling technology which could assist in speeding drug development is accelerator mass spectrometry (AMS). AMS analyses elemental isotopes at the single atom level; in the case of the radioisotope 14-carbon, femtogram to zeptogram quantities can be analysed. AMS is being increasingly used by the pharmaceutical and biotechnology industries to investigate the rate and routes of excretion of 14-carbon labelled drugs in humans. The sensitivity of AMS permits radioactive dose reductions for 14-carbon of up to one thousand-fold compared with conventional decay counting methods (nanoCurie as opposed to microCurie doses can be used).

One of the applications of AMS is in drug metabolism studies where blood, excreta and tissue samples obtained from human volunteers and/or patients administered microdose quantities of both 14-carbon labelled and drug substance are analysed. Microdose (human Phase 0) studies are performed to obtain information about the ADME/PK of new drug candidates prior to committing large resources to a full scale of Phase I study. Microdose studies should be part of the late stage discovery process especially as an aid in candidate selection. Microdose studies provide no safety and efficacy information about a candidate drug but do provide metabolism information at sub-pharmacological doses.

A fundamental question regarding microdose studies conducted in the USA is whether or not these studies would/could be covered by the 21CFR Part 361 regulation. This question arises because (a) for both AMS and PET, radioisotope administration is required and (b) the administered doses are sub-pharmacological. The key issue for adoption of the microdosing approach is a 'light' regulatory touch.

In my presentation, I would;

- ?? Highlight the drug dose and radioactivity limits used for microdose studies in Europe
- ?? Suggest a simple toxicology package to support microdose studies including a review of the EMEA Position Paper on 'Non-clinical Safety Studies to Support Clinical Trials with a Single Microdose'
- ?? Make proposals on how 21 CFR Part 361 might be amended to accommodate microdose studies on novel drug candidates

The FDA is to be commended for calling this meeting and to being open to new drug development approaches. As one of the instigators of the microdose concept, it is our view that human studies conducted under a revised 21 CFR Part 361, would greatly assist in accelerating drug development.

Presentation 10 minutes
time