



AccuSampler Standard - Automated Blood Sampling for ADME studies

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Abstract

The DiLab AccuSampler® is a fully automated system for blood sampling and injection of test compounds in freely moving animals. Use of the AccuSampler complies with and facilitates the implementation of many aspects of the “3R’s” in that of reduction and refinement. The system is in routine use in the pharmaceutical industry world wide and offers the following benefits: Better quality of results, Unattended operation, Flexible design, Stress free environment for animals, Low operating cost, and detailed documentation of the actual sampling procedure.

Key words

Automatic blood sampling system; ADME study; animal experiment

Article history

Received 30 March 2009; Accepted 12 May 2009

Publication data

Pages: 3; Tables: 0; Figures: 2; References: 3; Paper ID 1608-2281-2009-09020156-03

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Introduction

The **DiLab AccuSampler®** is a fully automated system for blood sampling and injection of test compounds in freely moving animals. Use of the AccuSampler® complies with and facilitates the implementation of many aspects of the “3R’s”: (1) **Reduction**: The AccuSampler® can greatly reduce the number of animals used since several samples can be drawn from the same animal as opposed to using multiple animals for one time point. (2) **Refinement**: The animals are undisturbed and do not experience stress during the automatic sampling procedure. This increases animal welfare as well as reduces potential interferences with hormone levels or blood glucose. The 3R Research Foundation, which is the Swiss platform for 3R alternative laboratory methods, is a member of ECOPA (European Consensus Platform for 3R-Alternatives to Animal Experimentation).

The AccuSampler® is the result of more than

fifteen years of research and has been developed in close collaboration with leading pharmaceutical companies. The system is in routine use in the pharmaceutical industry world wide and offers the following benefits: Better quality of results, Unattended operation, Flexible design, Stress free environment for animals, Low operating cost, and detailed documentation of the actual sampling procedure.

Performance

The AccuSampler® typically provides far more accurate data than manual procedures. This is due to the stress free environment for the animal, precise drawing and injection rates, as well as an exact, user defined, volume of waste blood being withdrawn at every sampling point. It is a valuable tool for pharmacokinetic, metabolism, toxicology and safety studies in rats. Good results have also been obtained

in other animal species including guinea pigs.



Fig 1. Automated system for blood sampling and injection of test compounds

Technical Description

A displacement pump handles the blood sampling with great accuracy and precision. Built in pressure sensors allow for the verification of the sampling process. The AccuSampler® Standard is

equipped with a 32 position rack for 1 ml plastic sample tubes. Custom rack types are available on request. The collected samples can be cooled if desired. The system has two separate liquid flow paths. The injection flow is operated with a syringe pump through which test formulations can be injected according to any desired time protocol. It is possible to perform bolus injections as well as a continuous infusion.

The AccuSampler® also presents the option of Dual Sampling e.g. two samples taken simultaneously from two different vessels - for instance before and after the liver. For dual sampling the AccuSampler® is equipped with two completely separated tubing systems and dual sample racks, with no risk for cross contamination.

The animal is connected to the AccuSampler® through a surgically implanted catheter leading to a stainless steel swivel mounted on a balanced lever arm. The swivel makes it possible for the animal to turn without twisting the catheter. The animals can move freely during the study with access to food and water. Samples can be taken and injections performed without disturbing the animal. All steps in the sampling procedures are monitored and logged by the AccuSampler® Software.

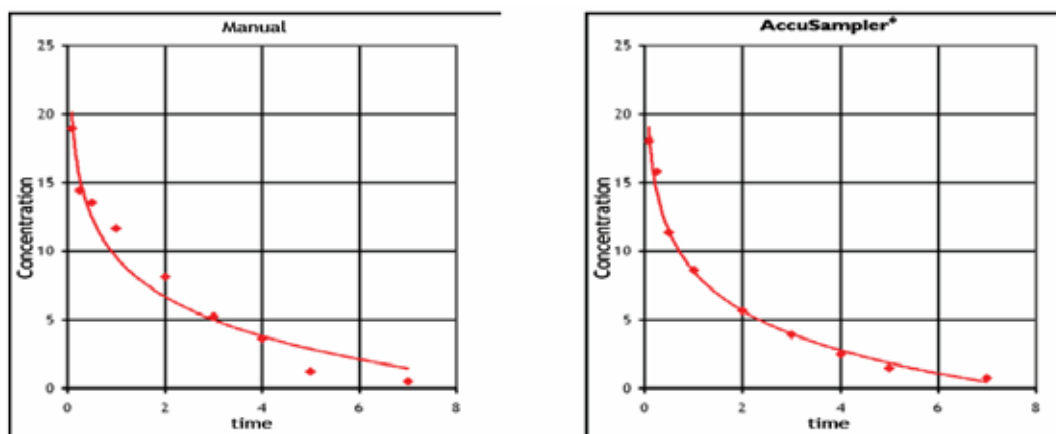


Fig 2. Manual sampling compared to automatic sampling with the AccuSampler®. The AccuSampler® provides results with very high accuracy.

Several options are available for the AccuSampler® Standard. These include: (1) Single or dual syringe infusion pump for drug infusion and/or saline flush. (2) The ability to split samples into multiple vials at each time point. (3) The ability

to perform dual sampling from two different vessels.

AccuSampler from a CRO Perspective

Ethical The number of animals used on an

AccuSampler study is one third of that used on a conventional study. Instead of groups of 9 males and 9 females, groups of only 3 males plus 3 females are required. Studies with drug candidates with difficult pharmacokinetic profiles, such as rapid liver metabolism, would require far fewer animals than conventional study.

Scientific Quality of blood samples is improved., Better profile can be obtained. Samples collected from the same animals, reduces inter-animal variability problems. The AccuSampler and associated data handling software are GLP compliant. Handling / moving animals around can induce changes in a number of important hormones. With AccuSampler, it is possible to obtain a true picture of the diurnal variations in, for example, growth hormone levels. Using conventional methods, this would be extremely difficult to achieve and would use many more animals.

Economic Amount of manpower required is

reduced. Surgery is relatively simple, although a little more time consuming in the initial phase (15-30 minutes per animal). This is more than compensated for by easier blood sampling procedure, any time, day or night, without any personnel needing to be present. For a CRO to be competitive, they need to be “up-to-date” with new technologies and offer these as a service.

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