IAA

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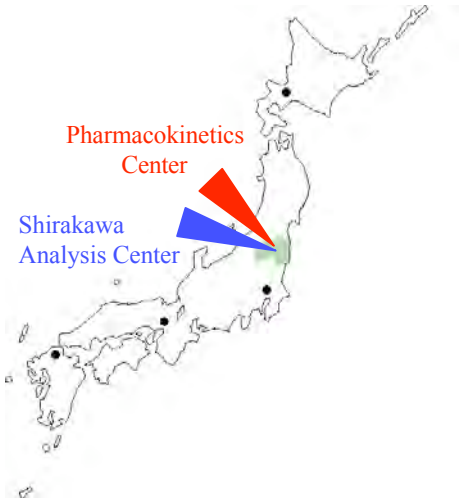
Shirakawa Analysis Center

Motomiya Pharmacokinetics Analysis Center

History of IAA



1999 March : Establishment of Institute of Accelerator Analysis Ltd. (IAA)

2000 April : Start of operating business for radiocarbon dating by beta ray counting methods
Start of marketing for radiocarbon dating by AMS analysis
November : Completion of Shirakawa Analysis Center (IAA-SAC)
December : Install of AMS machine (Pelletron 9SDH-2) in IAA-SAC

2001 February : Start of radiocarbon dating with AMS in IAA-SAC
May : Start of sales for dating by AMS analysis at IAA-SAC
August : Start of sales for dating by beta ray counting method at IAA-SAC
July : Start of sales and marketing for determination of 14C-labeled drug in biological amples by AMS analysis

2004 March : Agency agreement with Daiichi Pure Chemicals Co. Ltd. In pharmacokinetic studies
August : Start of construction of Motomiya Pharmacokinetics Analysis Center (IAA-MPAC)

2005 January : Install of AMS machine (Pelletron 1.5SDH-1) in IAA-MPAC
February : Completion of IAA-MPAC
March : Start of AMS analysis for pharmacokinetic studies with AMS in conformity with GLP at IAA-MPAC
May : Completion ceremony for IAA-MPAC
July : Agency agreement with Fuji Biomedix Co. Ltd. in pharmacokinetic Studies

Achievements of Pharmacokinetics Division in IAA

2002 July : Examination of application of AMS analysis to pharmacokinetics study
Validation studies of analytical method with AMS & collection of fundamental data

2003 April : Introduction of AMS analysis at 17th JSSX Workshop in Tokyo (Proc. 17th JSSX Workshop, p93-98)
June : Measurement of Background levels in biological samples and another control samples
October : Validation studies of AMS analysis with monkey's plasma (Linearity, reproducibility, relationship with LSC)
Report about results of validation studies of AMS analysis at 18th JSSX Annual Meeting in Sapporo
(Proc. 18th JSSX Annual Meeting, p306)

2004 February : Study 1 (Mass Balance Study with animals)
March : Study 2 (Mass Balance Study with animals)
April : Study 3 (Mass Balance Study with animals)
September : Study 4 (Mass Balance Study with animals)
November : Study 5 (Complication of AMS analysis and LSC analysis in human mass balance study)
Reports about results of mass balance studies with animal and human at 19th JSSX Annual Meeting in Kanazawa
(Proc. 19th JSSX Annual Meeting, p349)

Message from CEO

The Institute of Accelerator Analysis Ltd., IAA, is a research and analysis style company to measure the three isotopes of carbon (^{14}C, ^{13}C and ^{12}C) in archaeological dating and biomedical research with an Accelerator Mass Spectrometry (AMS).

In recent years, AMS attracts attention in many fields, such as archaeological anthropology, cultural property science, geology, the space and earth science, new drug development, environmental science, and basic science. Our company concentrates most advanced knowledge and technology, and is founded to respond to the demand from the many fields.

Since AMS measures directly the amount of ^{14}C that is radioisotope contained in samples, the sensitivity of AMS is 1,000 or more times higher than the conventional beta ray counting methods (liquid scintillation counter etc.). AMS can perform archaeological dating of higher precision, and its measurement is possible in few quantities of precious samples.

Moreover, AMS is capable of measuring the ^{14}C-labeled drug concentration on very low radioactivity levels in the various biological samples, such as plasma, urine, faeces, tissue/organ, and HPLC eluate etc. Comparing to the conventional methods, AMS becomes possible to reduce or less to 1/1,000 the amount of radioactivity dose to human volunteers in pharmacokinetics studies of new drug candidates. We think that there is a big advantage from points, such as handling and waste processing of the safety of dosing to the man, and environmental pollution.

In February 2005, Motomiya Pharmacokinetics Analysis Center will be established at Motomiya in Fukushima, Japan. We will address the other fields such as in-vitro studies in early stage (screening stage) of development of new drug as well as measurement drug concentration in biological samples.

We believe that IAA can contribute to society widely through AMS. We make constant efforts to offer a fully analytical services which are attached to expectations, considering with the working member and researchers.

Takao Mutsui
President and CEO

AMS Analysis of ^{14}C-labeled drug in biological samples

AMS is a very sensitive analytical method and is used to measure ^{14}C in various biological samples, such as plasma, urine, feces, tissue as well as HPLC eluate. AMS enable to measure the drug concentration on very low radioactivity levels which were not detected by the conventional beta ray counting method (such as LSC etc.).

At IAA, the validation studies of AMS analysis had been carried out with biological samples of human and animals, and the linearity, accuracy, precision, reproducibility and lower limit of quantification had been validated. Now, we measure the concentration of ^{14}C-labeled drug in biological samples such as plasma, urine, and feces obtained from human or animals as well as ^{14}C concentration in HPLC fractions to analyze the metabolites. We also examine application of AMS analysis to in-vitro studies such as radio receptor assay.

Characteristics of AMS Analysis

1. Very sensitive analysis and low limit of quantification
   Dosing radioactivity can be decreased.
2. Microanalysis
   Analyses of precious samples are possible.

Mass Balance Studies

AMS enables to analyze ^{14}C contents in plasma, urine, feces, as well as recovery rate of radioactivity, even if a ^{14}C-labeled drug of less than 100 nCi is administered to human or animal.

ADME Analysis

^{14}C concentrations in Tissue/Organ

Measurement of Protein Binding Rate

Microdosing Studies

To select drug candidates in early stage of drug development, pharmacokinetics data are obtained from human administered 1/100 of the dose to yield a pharmacological effect and less than 100 μ g.

HPLC Metabolite Profiling

Immunoassay Studies

Analysis of antibody-antigen interaction by using ^{14}C-labeled compound of less than 1dpm (0.45pCi).

Receptor/Ligand Binding Studies

Dating

- Archaeological analysis
- Geological analysis

Environmental

- Analysis of seawater
- Measurement of decomposition rate in biodegradable plastics

Analytical Process

Pre-discussion & Protocol

Protocol is issued after sufficient discussion with the Sponsor.

Partial Validation & Sample Preparation

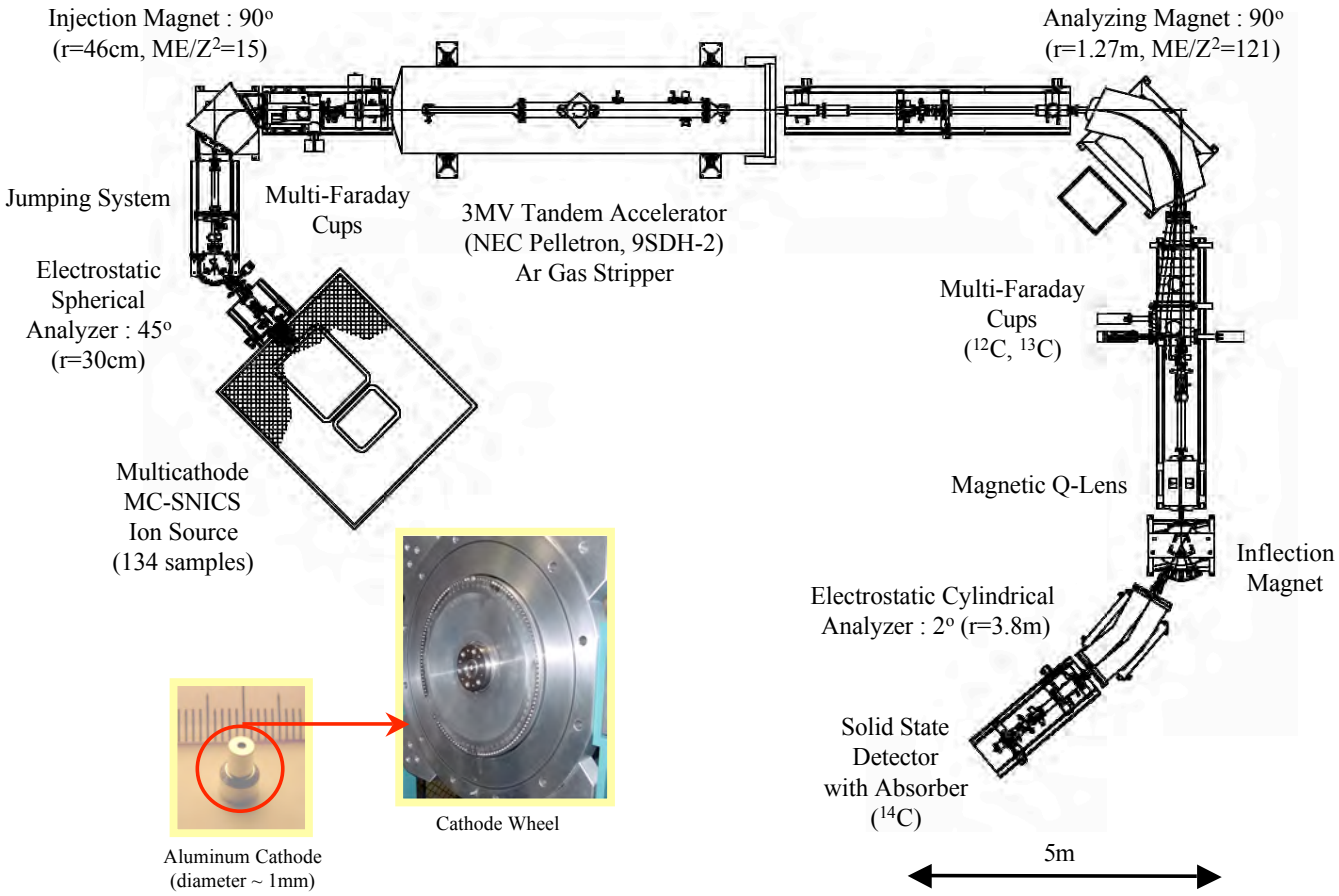
Full Validation had been carried out. Depending on the characteristics of test compound, a partial validation will be performed before analysis. Especially, we examine whether sample preparations such as dilution, extraction, collection and combustion are appropriate. All samples are transferred into graphite through serial oxidation and reduction reactions.

AMS Measurement

A maximum of 134 samples including standard and process control samples are measured in the same lot. The validity of AMS measurement is judged from that both the standard samples and process control samples meet the acceptance criteria.

Final Report

Final report is submitted after fully discussion with the Sponsor using a draft final report.


Injection Magnet : 90º
(r=46cm, ME/Z²=15)
Analyzing Magnet : 90º
(r=1.27m, ME/Z²=121)
Jumping System
Multi-Faraday Cups
3MV Tandem Accelerator
(NEC Pelletron, 9SDH-2)
Ar Gas Stripper
Electrostatic Spherical Analyzer : 45º
(r=30cm)
Multi-Faraday Cups
(¹²C, ¹³C)
Multicathode MC-SNICS Ion Source
(134 samples)
Magnetic Q-Lens
Inflection Magnet
Electrostatic Cylindrical Analyzer : 2º (r=3.8m)
Solid State Detector with Absorber
(¹⁴C)
Cathode Wheel
Aluminum Cathode
(diameter ~ 1mm)
5m


Detector (¹⁴C)
Ion Source
Electrostatic Accelerator
IAA-AMS 3MV Tandem Accelerator

April 2005