Agilent RapidFire 360 High-throughput Mass Spectrometry System

Innovative Integrated Technology

The Measure of Confidence

Agilent Technologies

Streamline workflows and eliminate bottlenecks

By combining the accurate mass capabilities of time-of-flight (TOF) mass spectrometry and the high-throughput processing speeds of the Agilent High-throughput RapidFire technology, the RapidFire 360 revolutionizes *in vitro* ADME analysis. The Agilent RapidFire 360 synergizes the unprecedented sample processing speed of RapidFire with the high resolution of TOF mass spectrometry, thereby eliminating the lengthy method development required for the analysis of metabolic stability, plasma protein binding, PAMPA, Caco-2 and other *in vitro* ADME assays. Without the bottleneck of method optimization during ADME assay analysis, workflow is significantly streamlined and researchers are free to concentrate on other tasks. Data turnaround is achieved at exceptional speeds because the RapidFire 360 processes a 96 well plate in about 15 minutes, without any compromise to data quality.

The RapidFire 360 Mass Spectrometry system eliminates the need for sample preparation and delivers samples to the mass spectrometer at unprecedented speeds.

Seamless integration with Agilent TOF

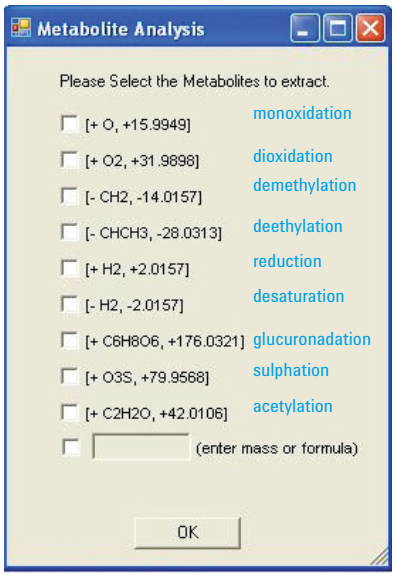
The Agilent RapidFire 360 High-throughput system fully integrates with Agilent's Mass Hunter software via the RapidFire Integrator software. Large volumes of data are easily processed and presented in a format that is straightforward and efficient.

Reduce method development time

The RapidFire 360 couples the unprecedented sample processing speed of RapidFire with the high resolution and mass accuracy of TOF mass spectrometry, eliminating the lengthy triple quadrupole method optimization typically required for applications such as metabolic stability, permeability and other *in vitro* ADME assays.

Agilent reliability, of course

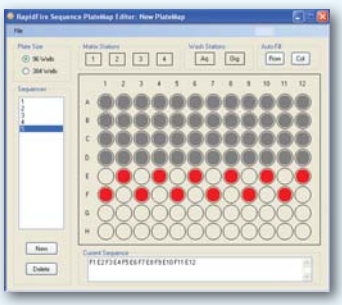
Agilent's commitment to innovation and performance improvement continues to produce new instruments with industry-leading speed, sensitivity, and performance. But one thing always remains constant: robust, Agilent-reliable performance and ease-of-use.

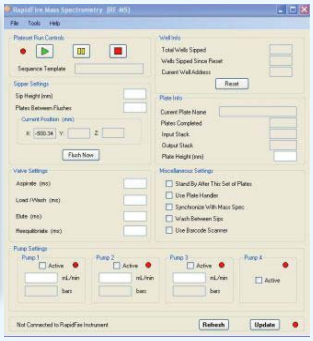


Automatically identify metabolites without a priori knowledge of compound structure or metabolism.

RapidFire software simplifies and automates data analysis

Agilent RapidFire 360 software enables a broad range of capabilities. The user interface is easy to use and network enabled, allowing users to monitor instrument progress from their desktop. The plate map editor enables sequenced-based functionality. Injection in any plate configuration allows for custom design of sequences which may be saved. RapidFire Integrator transforms direct mass spectrometry data output into data files compatible with standard LIMS and other databases.

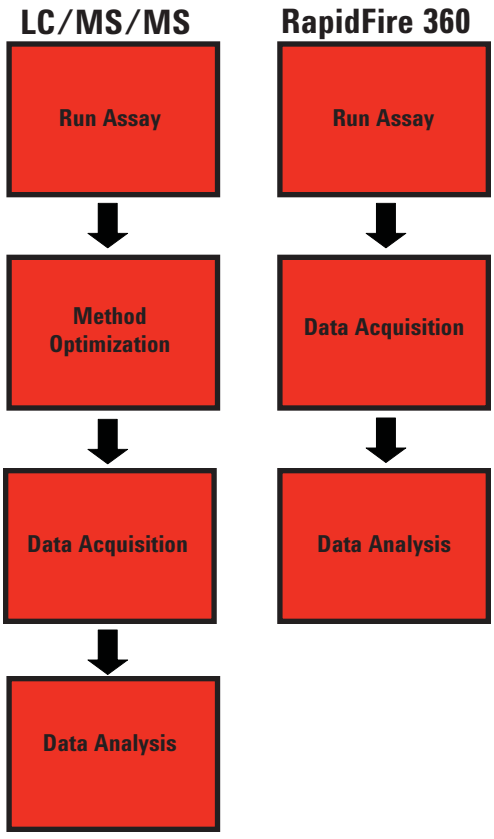




Robust, reliable results at u

Agilent's proprietary RapidFire 360 technology provides researchers with a significant competitive edge by decreasing the time required for screening. Each sample is processed in just six to ten seconds, yielding much faster throughput than traditional mass spectrometry-based methods. A single 384 well plate can be read in under 40 minutes.

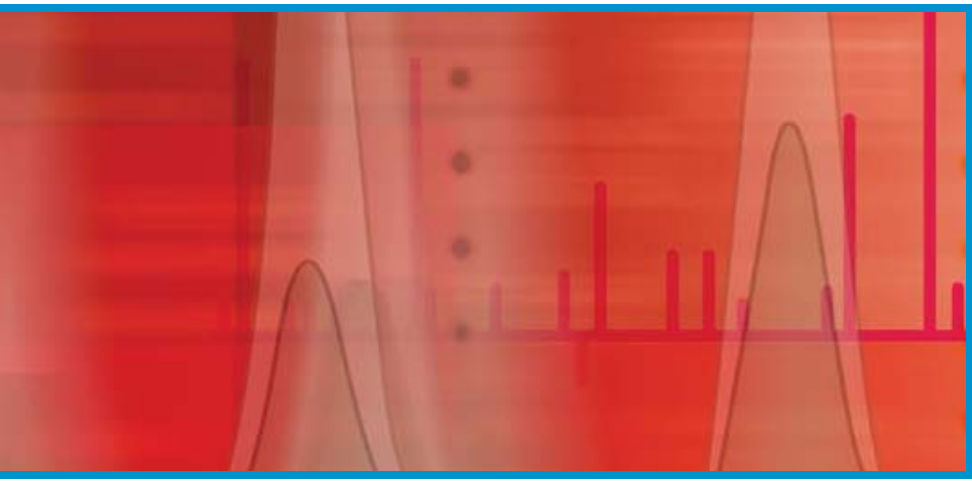
The RapidFire 360 system requires no up-front sample preparation. The system samples directly from quenched assay plates without the need for offline solid phase extraction or any other sample desalting or preprocessing. By taking advantage of the full scan acquisition capabilities of TOF mass spectrometry, the RapidFire 360 system shortens sample processing times. Reducing the method optimization that is required on a triple quadrupole mass spectrometer saves time and streamlines workflows for a variety of *in vitro* ADME assays.



nparalleled throughputs

"We developed the RapidFire 360 to address the challenges facing researchers in the biopharmaceutical industry. The RapidFire 360 solution enables significant streamlining of workflows and gives researchers a competitive edge in drug discovery."

Dr. Can Özbal, Director RapidFire Operations, Agilent Technologies



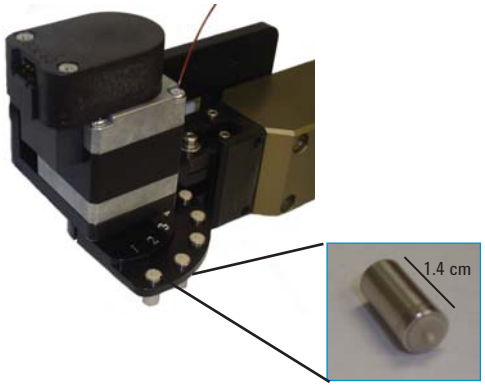
FAST EFFICIENT ANALYSIS WITHOUT COMPROMISES

Unattended 24-hour operation

The RapidFire 360 system incorporates a variety of features that enable unattended, 24-hour operation, permitting researchers to dedicate time to other tasks and process samples on the instrument overnight without the need for operator supervision. Automated cartridge changing hardware can extend unattended operating hours or be loaded with multiple packing materials for method development applications. Integrated optical sensors automatically detect fluid flow and the software flags any aberrant samples.

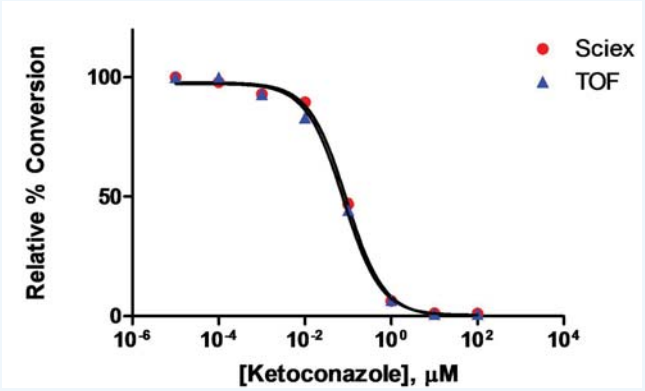
Solid phase extraction cartridges

RapidFire cartridges are available in a variety of chemistries including: C4, Cyano, C18, Phenyl, C8, HILIC, and custom packing materials. The assay development cartridge cassette allows for the use of six different packing materials enabling analysis by multiple chemistries in a method development mode.



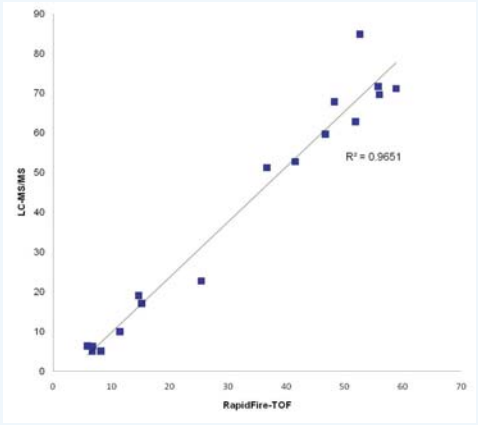
Combine existing workflows with revolutionizing speed

DRUG-DRUG INTERACTION:
CYP inhibition with FDA recommended drug probes



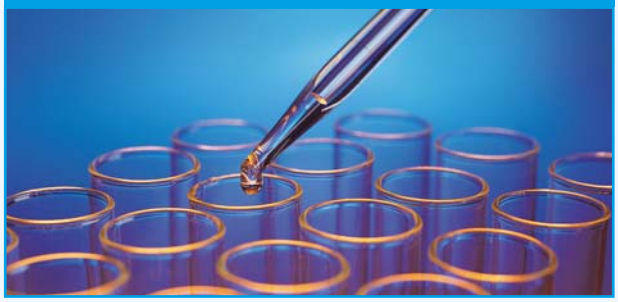
CYP3A4 Inhibition: An IC_{50} curve for ketoconazole, a known inhibitor of CYP3A4, was run using human liver microsomes with standard assay conditions. Samples were then analyzed using the RapidFire 360 or traditional LC/MS/MS methods. The IC_{50} curves and calculated IC_{50} values were identical between the two analysis platforms. The RapidFire 360 sample analysis cycle time was 9.5 seconds/sample producing a 15-fold increase in speed and throughput compared to LC/MS/MS.

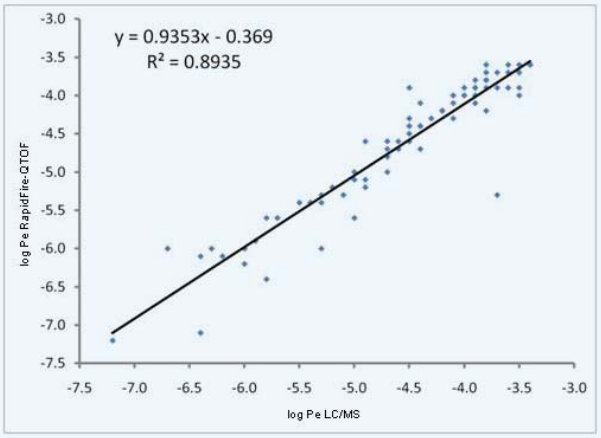
METABOLIC STABILITY:
Determine *in vitro* intrinsic clearance



A chemically diverse set of commercially available drug compounds were incubated with human liver microsomes using standard metabolic stability assay conditions and quenched with an equal volume of acetonitrile containing internal standard. Samples were then analyzed using the RapidFire 360 or traditional LC/MS/MS methods. Correlation results for fast and intermediate half-lives (less than 60 minutes) are shown. The metabolic half-life values were essentially equivalent between the two platforms (R^2 greater than 0.95). In addition to the greater than 13-fold decrease in analysis cycle time of the RapidFire 360 system, these results indicate that the triple quadrupole method optimization can be eliminated for the metabolic stability assay, thus providing additional workflow efficiency.

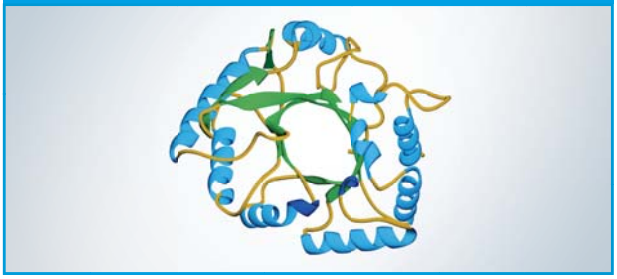
PERMEABILITY:
PAMPA and cell-based assays



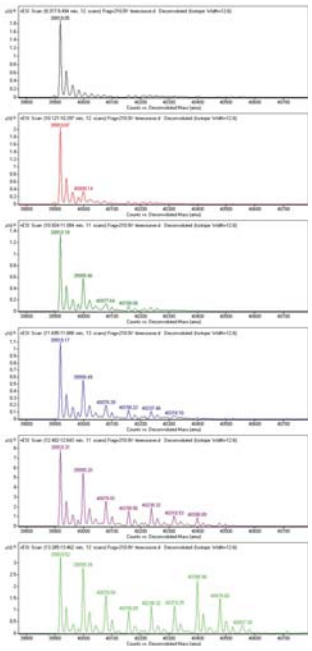


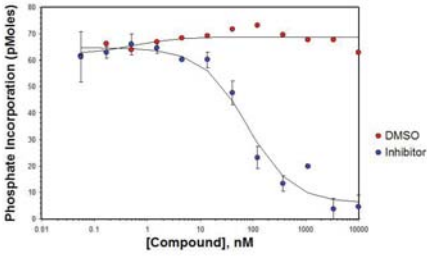
PAMPA: A chemically diverse set of drug discovery lead compounds (88) was assayed using standard PAMPA assay conditions. Samples were then analyzed using the RapidFire 360 or traditional LC/MS/MS methods. The calculated log Pe values correlated very well between the two analysis platforms. In addition to the greater than 15-fold decrease in analysis cycle time of the RapidFire-MS system, these results indicate that the triple quadrupole method optimization can be eliminated for this permeability assay thus providing additional workflow efficiency.

WHOLE PROTEIN SCREENING:
Complex kinetics, modifications



RapidFire 360 was used to analyze an intact 39 kDa protein at sustained throughputs of 10-12 seconds/sample. This system was able to quantitate multiple (in this case eight) phosphorylation states on the full length native protein. Sequential phosphorylation over a time course is shown. An inhibition study was conducted and the IC_{50} value was determined. These results illustrate the ability of the RapidFire 360 system to conduct label-free screening of whole protein kinase assays.





Experience clearly better productivity and save resources, too

The Agilent RapidFire 360 High-throughput Mass Spectrometry system is engineered using precisely controlled nanofluidics. The result is a significant decrease in solvent usage and a reduction in overall waste including hazardous solvents that require difficult disposal processes.

Contract research services

The Agilent RapidFire Assay Analysis Service increases your lab's productivity while preserving your assay method integrity. Simply send Agilent your quenched ADME assay plates and the analysis will be performed using RapidFire-MS, returning data results within 3 days. Analysis of traditional ADME assays (i.e. CYP inhibition, metabolic stability, and permeability) or customized analysis services are available.

The Agilent Value Promise: 10 years of guaranteed performance

In addition to our continually evolving products, Agilent offers the industry's only 10-year value guarantee. Agilent guarantees you at least 10 years of instrument use from your date of purchase, or we will credit you with the residual value of that system toward an upgraded model. It's our way of assuring you of a safe purchase now and protecting your investment.

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