Quantitative Whole-Body Autoradiography (QWBA)

Charles River offers a full range of drug metabolism and pharmacokinetic studies in support of drug candidate selection or regulatory submission. Our skilled pharmacokineticists, surgeons, toxicologists and bioanalytical chemists work together to design and interpret both in vitro and in vivo components of your metabolism studies, which can vary based on your program goals.

Elucidation of drug distribution in preclinical species can help identify potential target tissues for toxicity or confirm suitable exposure of the therapeutic target. Charles River can support you in procuring this information with the effective design, conduct and delivery of quantitative whole-body autoradiography (QWBA) studies as part of our preclinical drug metabolism service.

QWBA is now regarded as the technique of choice for determining the distribution of drug-related material in laboratory animals. The response of the phosphor screen to radioactivity has been shown to be quantitative over at least five orders of magnitude and the high-resolution (50 microns) digital image obtained can be enlarged to provide greater depth and detail of distribution across and within the tissues or organ of interest.

Tissue Distribution and Histology Equipment
Charles River offers the Typhoon™ FLA 7000 scanner (GE Healthcare), a fast laser scanner optimized for quantitative phosphor imaging, ECL Plus Westerns, visible single fluorescence and gel documentation. It offers high speed (20 x 40 cm gel in 2.5 minutes) with high sensitivity (up to 25 μm resolution) for accurate quantification of closely spaced targets and full visible fluorescence with 473/532/635/650 nm excitation and up to 25 μm resolution for gel and blot imaging.

In addition, we also offer the CryoJane® Tape-Transfer System (Leica), an add-on for existing cryotomes that eliminates the problems normally encountered during cutting and staining frozen tissue sections by utilizing cold adhesive tapes and slides. This process produces a frozen section with minimal ice crystal artifact and the cellular structures preserved.

QWBA Applications
- Tissue distribution
- Target organ/tissue validation
- Correlation with histopathology
- Placental transfer
- Penetration of blood-brain barrier
- Tumor penetration
- Support of micronucleus test
- Melanin binding
- Human dosimetry calculations

Isotope Detection
- Carbon-14
- Gadolinium-153
- Iodine-125
- Phosphorus-32
- Strontium-89
- Sulfur-35
- Tritium
- Other beta or gamma emitters
Microautoradiography
Microautoradiography enables the localization of the distribution of drug-related material at cellular or subcellular levels. Tissues of interest are selected either from previous QWBA images or target tissues indicated from toxicology findings. The images generated from microautoradiography allow the operator to correlate in vivo sites of specific binding with therapeutic activity or observed toxicity to gain information on the mechanism of action involved. Tissues collected from animals previously dosed with a radiolabeled test article are sectioned onto glass slides with minimal processing in order to maintain structural integrity. The sections are treated with a photographic emulsion to allow for the visualization of deposited silver grains, which are indicative of distribution of radioactive material.

Charles River also offers microautoradiography assays using a tape transfer system that allows collection of whole-body sections, thereby enabling a direct correlation of QWBA with histopathology.

MALDI-MSI
Offered in collaboration with ImaBiotech, MALDI-MSI (Matrix Assisted Laser Desorption/Ionization Mass Spectrometry Imaging) can provide an additional output for QWBA studies. By scanning QWBA sections for the presence of parent compound and metabolites/degradants MALDI-MSI can provide information to characterize the nature of the radioactive components detected in QWBA imaging. In addition, MALDI-MSI can provide a label-free imaging alternative for the detection and localization of xenobiotics and their metabolites.

The technique is ideally suited to assessing the intra-organ distribution of drugs and their metabolites. MALDI-MSI can be successfully adapted to provide whole-body images in small rodent species. Furthermore, using proprietary Quantinetix™ software, quantitative data can be produced.

LESA-MS
In addition to MSI, Liquid Extraction Surface Analysis Mass Spectrometry (LESA-MS) combines a micro-liquid extraction from a solid surface followed by nano-ESI coupled with MS analysis of the generated ions to gain information from tissue sections. Information from the whole body animal section can be obtained by liquid extraction of analytes from the solid surface followed by nano-electrospray ionization. It can be combined with any type of mass spectrometer to gain information by accurate mass or SRM analysis. Whereas QWBA relies on the use of radiolabeled drugs and is limited to total radioactivity measured, LESA-MS can provide drug- and metabolite-specific distribution information.