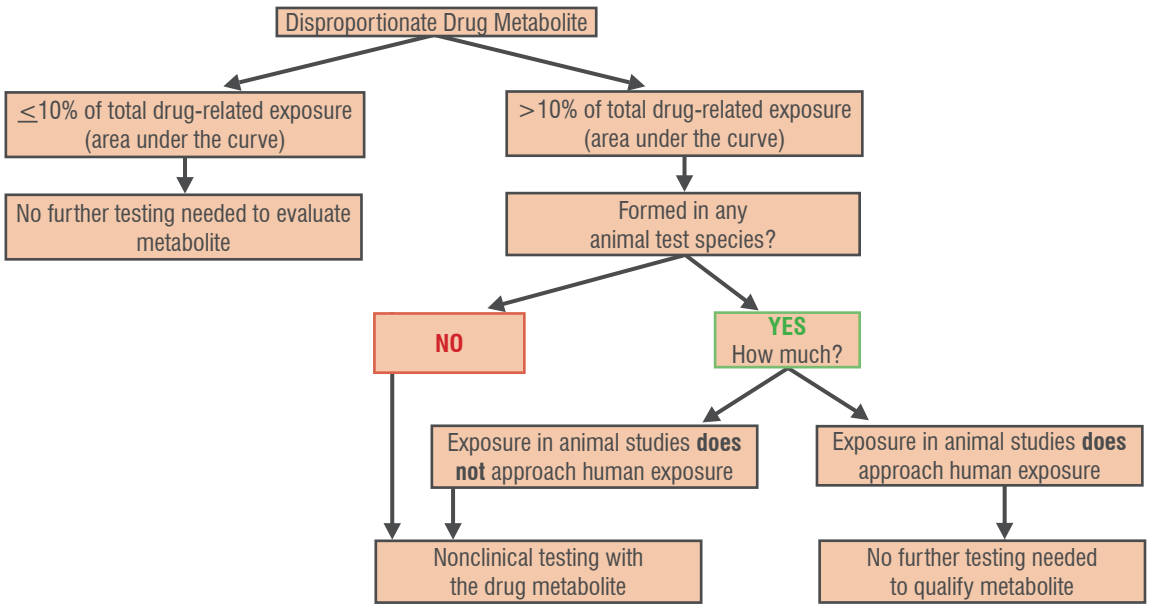
Full-Service Offering to Comply with Metabolites in Safety Testing (MIST) Regulations

Development of drug candidates with high quality data in regulated environment is crucial for patient safety. Q² Solutions understands the importance of delivering it in all stages of the development cycle.

Q² Solutions routinely supports clients in conducting metabolite profiling and identification of Human Exploratory studies from SAD and MAD Phase I studies. Our biotransformation group routinely conducts both preclinical (in vitro, in vivo, RI, phenotyping, Radiolabelled ADME studies etc.) and clinical (Exploratory, Radiolabelled Human ADME) metabolite ID and profiling studies.

According to the FDA MIST guidance – *"Generally, metabolites identified only in human plasma or metabolites present at disproportionately higher levels in humans than in any of the animal test species should be considered for safety assessment. Human metabolites that can raise a safety concern are those formed at greater than 10 percent of total drug-related exposure at steady state…"*.

Disproportionate Drug Metabolite Flow Diagram*



Expertise in Human Exploratory Studies

Our scientists in the Biotransformation group have an excellent reputation in conducting metabolite profiling and metabolite identification studies with high quality deliverables. Identification of circulating metabolites and finalizing structures is crucial, especially for disproportionate and unique circulating metabolites found in human samples. We have state of the art instrumentation and processing software to support the identification of metabolites. Our group is strengthened with scientists each having more than 15 years of average experience in identification of metabolites.

*Safety Testing of Drug Metabolites (Rev 2) – FDA Guidance, Mar 2020

Q² Solutions-Hypha Collaboration

Q² Solutions and Hypha Discovery have a successful track record in combining their capabilities to provide an end-to-end project managed solution to clients, which addresses the challenges in identification of metabolites and accessing scalable quantities for further characterization.

As one of the largest bioanalytical and ADME service providers in the world, Q² Solutions offers industry-leading expertise and resources in support of routine and challenging biotransformation studies, including metabolite profiling and metabolite identification by LC/MS. Complementing these services is Hypha's expertise in the scalable synthesis, purification and structure elucidation of metabolites of drugs. Applying a comprehensive portfolio of methods, including microbial and liver S9 / microsomal biotransformation methods, chemical synthesis, and recombinant enzymes, Hypha has the ability to produce gram amounts of synthetically challenging phase 1 and phase 2 metabolites. Combined with strong capabilities in purification chemistry and structural elucidation using state-of-the-art NMR spectroscopy, Hypha is able to deliver a world class service to clients requiring access to metabolites for definitive MetID and for biological testing.

Addressing Challenges in Disproportionate Metabolite Identification and production

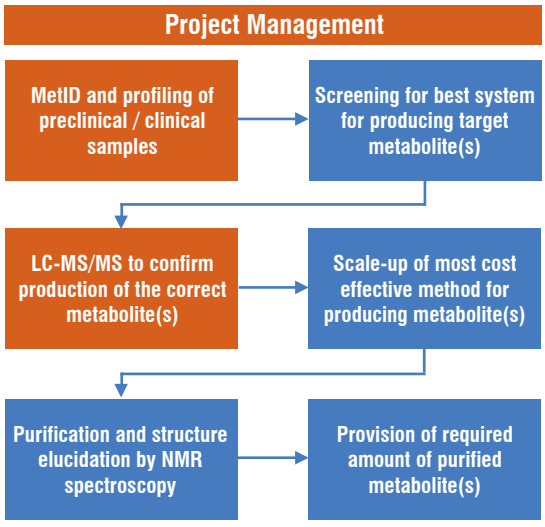
Due to limitations with LC-MS/MS instrumentation and fragmentation techniques, identification of the structures of disproportionate metabolites is not always possible, especially where definitive identification of the position of modification is required. To address this challenge, Hypha employs NMR spectroscopy to elucidate structures from data acquired using state-of-the-art instrumentation, including the application of cryoprobe technology. Hypha is able to purify metabolites from biological matrices for structure elucidation, or where there is limited availability of biological samples from a human study, scientists at Hypha can employ a number of different techniques to synthesize the desired metabolites. Larger quantities of disproportionate metabolites may also be needed for toxicological evaluation and DDI studies in order to comply with MIST guidelines. Hypha's methods are scalable in order to provide gram amounts of all commonly observed metabolite types such as those derived from both CYP and non-CYP enzymes, including conjugates such as glucuronides and sulfates.

All Services Under One Contract with Q² Solutions

In order to provide a seamless solution to our clients, Q² Solutions co-ordinates with Hypha to project manage all the various elements of the study, including producing one consolidated report and issuing all quotes and invoices.

Complete service offering to comply with MIST regulatory guidance

- Metabolite ID and profiling of preclinical and clinical samples
- Metabolite synthesis – screening and scale up from Hypha Discovery
- LC-MS/MS confirmation of presence of metabolites using clinical plasma samples
- NMR spectroscopy to finalize structure produced in scale up by Hypha Discovery
- Sufficient metabolite quantities for future studies



Learn more about how we help our customers at
Q2LabSolutions.com/Bioanalytical-ADME-Laboratories

Contact us

Toll free: +1 855.277.9929
Direct: +1 919.998.7000
International: +44 (0) 1506 814000
Website: www.Q2LabSolutions.com