charles river

DISCOVERY

Custom Metabolite Synthesis and Isotopic Labelling Service

Service Advantages

- Rapid delivery of results
- Expert data analysis and recommendation
- Fee for service (FFS) models
- Full time equivalent (FTE) models
- Experienced scientific staff
- Charles River's end-to-end platform
- Capacity and flexibility to meet client timelines

In 2008, the FDA released guidance for drug metabolite safety testing (MIST), highlighting the importance of metabolite toxicity testing in the drug development process. Drug toxicity accounts for roughly 40% of clinical drug failures[1] and contributes to the high drug attrition rates and spiralling costs associated with drug discovery today. The FDA has published guidelines[2] recommending that all human disproportionate drug metabolites (identified only in humans or are present at disproportionately higher levels in humans) accounting for >10% of total exposure are assessed in safety studies, including general toxicology, genotoxicology, embryo-fetal development toxicity, and carcinogenicity studies.

Custom Metabolite Synthesis

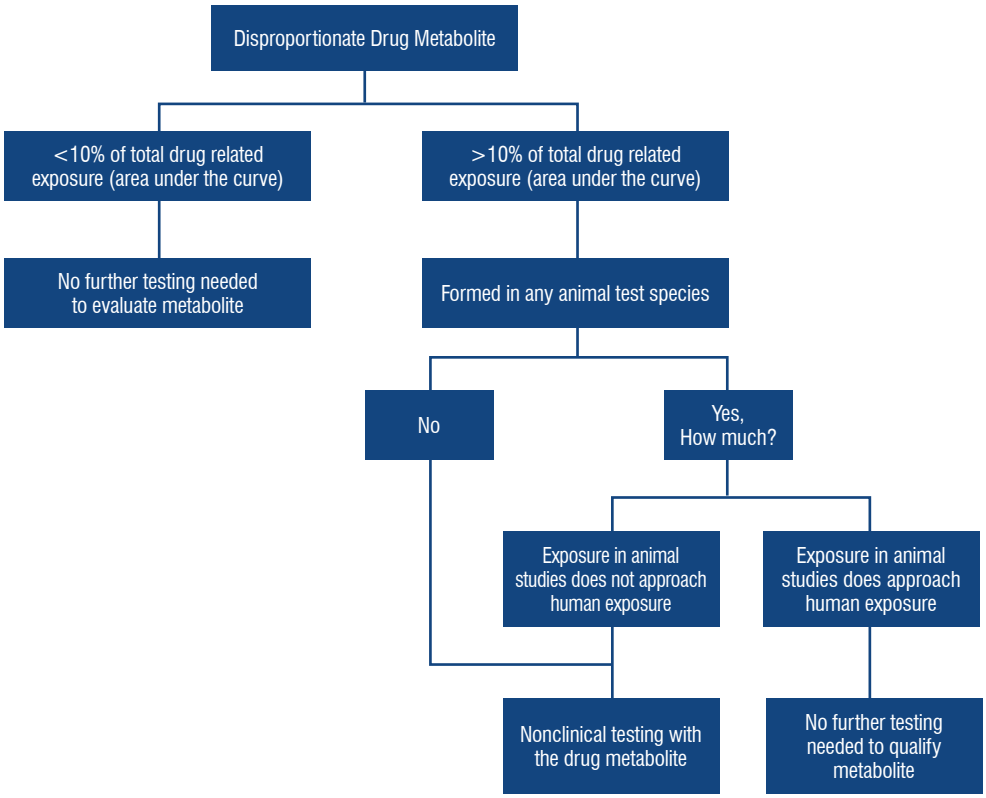
Charles River can provide a flexible custom metabolite synthesis service tailored to client needs. Where metabolic fates of APIs are known, we routinely design and execute multi-step synthesis with on-site state of the art facilities that deliver rapid results. If metabolic fates of APIs are unknown, we offer a range of options from targeted custom synthesis of putative metabolites, to screening an extensive panel of biomimetic oxidative and de-alkyation chemistries on full APIs. Whatever the question, our team of experts are on hand to offer advice and recommend solutions.

The custom synthesis of metabolites and putative metabolites comes with a comprehensive data package, with supporting analytical data provided up to GLP standard as required to facilitate regulatory submission. All materials are provided with a Certificate of Analysis specifying UPLC-MS purity and ^{1}H-NMR (^{13}C, ^{19}F, ^{15}N and ^{31}P-NMR as required).

Isotopic Labelling Services

Whether clients require an internal standard for quantitative analysis in a clinical study, need to determine metabolic routes and rates, or require an assay substrate molecule which releases a labelled product distinct from the endogenous product molecules present in a cell or tissue sample, we can provide a flexible custom stable isotopic labelling service for APIs. Our team of experts readily advise and offer solutions that account for likely sites of metabolism, minimizing the risk of subsequent loss of labelling within putative metabolites. We routinely design and execute multi-step synthesis that delivers for our clients, and with on-site state of the art facilities, we can provide rapid results.

Custom synthesis of stable isotope labelled materials comes with a comprehensive data package, with supporting analytical data provided up to GLP standard as required to facilitate regulatory submission. All materials are provided with a Certificate of Analysis specifying UPLC-MS purity, ^{1}H-NMR (^{13}C, ^{19}F, ^{15}N and ^{31}P-NMR as required) and a measure of isotopic enrichment ascertained by Q-TOF LC-MS.



References

[1] Nature Biotechnology volume 32 (1), 40-51, 2014

[2] https://www.fda.gov/downloads/Drugs/.../Guidances/ucm079266.pdf

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