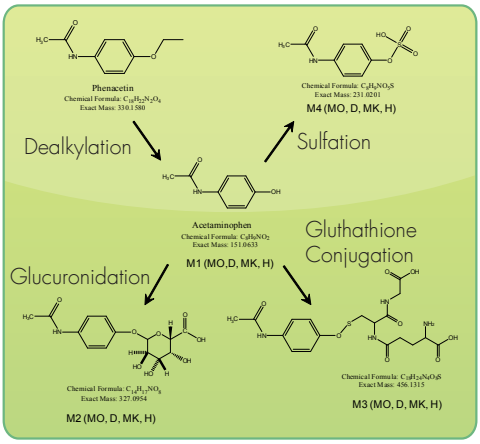
Nextcea

Drug Metabolite Identification Services for FDA IND/NDA Safety Assessments

Nextcea performs drug metabolism assays to identify and quantitate drug metabolites in animals and humans in compliance with FDA guidance for safety testing of drug metabolites

Biotransformation occurs via Phase I (aliphatic and aromatic oxidation, N-oxidations, dealkylations, reductions…) and Phase II (glucuronidation, glutathione, sulfation conjugations…) metabolism. The FDA encourages "the identification of differences in drug metabolism between animals used in nonclinical safety assessments and humans as early as possible during the drug development process[1]." Animals used in drug safety assessment should have systemic exposure to drug metabolites at least comparable to the major drug metabolites observed in humans.

Phenacetin metabolic pathway



In Vitro Assays

Nextcea offers a full range of in vitro services for drug metabolite identification and across-species profiling including incubations with hepatocytes, liver microsomes, S9 fractions, and recombinant human enzymes such as CYP450 isozymes (1A2, 3A4, 2D6, 2C8, 2C9, 2C19…), flavin monoxygenase isozymes, and UDP glucuronosyl transferases isozymes (UGT1A1, 1A10, 1A3, 1A4…).

In Vivo Assays

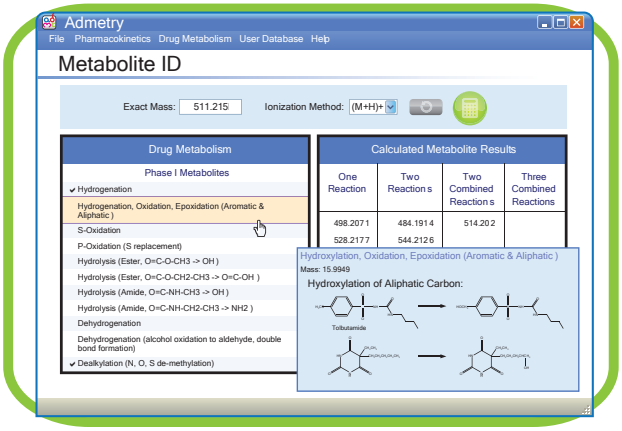
Nextcea also performs in vivo metabolite identification services across *any* animal species the client prefers. Animal and human biological in vivo samples can be provided by the client for metabolite identification. Alternatively, test compounds can be submitted directly to Nextcea and the animal dosing and sample collection will be coordinated at a partner animal facility.

Metabolite Synthesis

Nextcea synthesizes potential metabolites for structure confirmation and quantitation. The FDA recommended the synthesis and dosing of suspected toxic metabolite(s) to animals if they are found exclusively or in disproportionately higher levels in humans[1].

Study Design & Across Species Metabolite Analysis

Nextcea provides expertise in in vivo drug metabolism study design to meet the clients' drug development needs. Data is presented in a detailed report including drug metabolic pathways with across species comparison. Nextcea can conduct studies to confirm the structures of metabolites and develop assays to quantitate metabolites and determine exposure in humans and animals. Additionally, drug metabolism study results can be correlated with toxicological outcomes if desired by the client.



Nextcea employs proprietary bioinformatic software (Admetry®) to identify metabolites across different species.

About Nextcea, Inc.

Nextcea, Inc. is a drug development service company dedicated to optimizing efficacy and minimizing toxicity in all phases of drug development. Nextcea integrates cross-species ADME and biomarker studies with traditional PK/PD and TK/TD. In-house platforms include mass spectrometry LC-MS and LC-MS/MS (API-6500s and TripleTOF 6600), and proprietary pharmacokinetic and drug metabolism bioinformatics (Admetry®).

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1 Guidance for Industry: Safety Testing of Drug Metabolites. Pharmacokinetic Subcommittee at the Food and Drug Administration.

Metabolite Identification Services for Safety Assessment