

# Bioanalytics, Metabolomics and Pharmacokinetics Shared Resource (BMPK)

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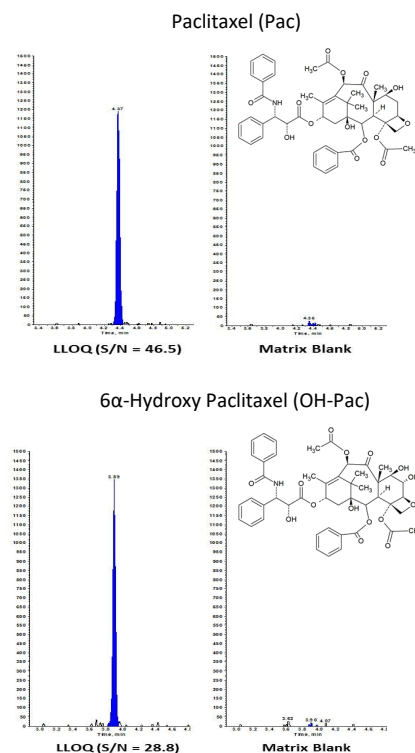
## Paclitaxel in Heparinized Human Plasma

(Sensitivity: 2.00 ng/mL)

BMPK has validated a highly sensitive liquid chromatographic tandem mass spectral assay (LC-MS/MS) for the analysis of paclitaxel (TAXOL<sup>®</sup>) and its active metabolite, 6 $\alpha$ -hydroxyl paclitaxel in heparinized plasma. Paclitaxel is a novel anti-microtubule agent that prevents microtubule disassembly and reorganization into a network essential for mitotic cellular function.<sup>1</sup> Currently, paclitaxel is approved alone or in combination with other chemotherapeutic agents for a variety of disease types. The validated method has been used to support a clinical trial conducted at Roswell Park Comprehensive Cancer Center entitled "Phase I Study of Ceritinib (LDK378), a Novel ALK Inhibitor, in Combination with Gemcitabine-Based Chemotherapy in Patients with Advanced Solid Tumors".

### Specifications and Validation Performance

<b>Matrix (Anticoagulant):</b>	Human Plasma (Sodium Heparin)
<b>Required Volume:</b>	100 $\mu$ L
<b>Preparation Procedure:</b>	Liquid/Liquid Extraction
<b>HPLC Column:</b>	C18
<b>Mobile Phase:</b>	Acetonitrile/Methanol with Acetic Acid
<b>Flow Rate:</b>	400 $\mu$ L/min
<b>Detection Type:</b>	Tandem Mass Spectral (MS/MS)
<b>Calibration Ranges:</b>	2.00 - 1,000 ng/mL for Pac and OH-Pac
<b>Calibrator Accuracy:</b>	100% (97.5 - 104%; n=5) for Pac 100% (96.3 - 105%; n=5) for OH-Pac
<b>Calibrator Precision:</b>	2.55% CV (0.924 - 4.69%; n=5) for Pac 2.95% CV (1.17 - 4.78%; n=5) for OH-Pac
<b>QC Concentrations:</b>	6.00, 75.0, 750 ng/mL for Pac and OH-Pac
<b>QC Accuracy:</b>	102% (99.6 - 105%; n=18) for Pac 101% (99.4 - 105%; n=18) for OH-Pac
<b>QC Precision:</b>	4.12% CV (2.77 - 5.12%; n=18) for Pac 3.42% CV (2.50 - 3.88%; n=18) for OH-Pac



### Human Pharmacokinetic Parameters of Paclitaxel<sup>1</sup>

<b>Recommended Dose</b>	100 - 175 mg/m <sup>2</sup> IV infusion over 1-3 hours every 2-3 weeks. Dosing is adjusted 45 - 50 mg/m <sup>2</sup> /week depending on the disease and combination treatment.
<b>Active Metabolite</b>	6 $\alpha$ -Hydroxy paclitaxel
<b>Metabolism</b>	CYP2C8 and CYP3A4 lead to three hydroxylated metabolites
<b>Drug Interactions</b>	Caution should be exercised when paclitaxel is concomitantly administered with known substrates or inhibitors of CYP2C8 and CYP3A4.
<b>Plasma Protein Binding</b>	89 - 98% (over the concentration range of 0.1 - 50 $\mu$ g/mL)

<sup>1</sup>Paclitaxel Patient Information, Mylan Institutional LLC, Revised 12/2018.

BMPK offers a wide range of bioanalytical and PK/PD modeling services to assist investigators in their basic research, preclinical, and clinical study objectives.

For information on services and pricing, contact **Wenjuan Zha, Ph.D.**, Associate Director at (716) 845-3258 or [Wenjuan.Zha@RoswellPark.org](mailto:Wenjuan.Zha@RoswellPark.org).