CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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CLINICAL PHARMACOLOGY REVIEW(S)

Office of Clinical Pharmacology Review

NDA Number (SDN)	218711 (SDN 1)
Link to EDR	\\CDSESUB1\evsprod\NDA218711\0000
Submission Date	10/06/2023
Submission Type	505(b)(2)
Brand Name	BEIZRAY
Generic Name	Docetaxel Injection
Dosage Form and Strengths	Injection solution containing 20 mg/mL of docetaxel in single-dose vials (80 mg/4 mL)
Route of Administration	Intravenous (IV)
Proposed Indications	• Breast Cancer (BC): single agent for locally advanced or metastatic BC after chemotherapy failure; and with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive BC • Non-small Cell Lung Cancer (NSCLC): single agent for locally advanced or metastatic NSCLC after platinum therapy failure; and with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC • Castration-Resistant Prostate Cancer (CRPC): with prednisone in metastatic castration-resistant prostate cancer • Gastric Adenocarcinoma (GC): with cisplatin and fluorouracil for untreated, advanced GC, including the gastroesophageal junction • Squamous Cell Carcinoma of the Head and Neck (SCCHN): with cisplatin and fluorouracil for induction treatment of locally advanced SCCHN
Applicant	Zhuhai Beihai Biotech Co., Ltd.
OCP Review Team	Dapeng Cui; Jason Moore (TL)
OCP Final Signatory	Stacy Shord

Table of Contents

List of Tables

1. EXECUTIVE SUMMARY

This application is a 505(b)(2) NDA submission by Zhuhai Beihai Biotech Co, Ltd., requesting the approval of Beizray (docetaxel) Injection, 20 mg/mL (80 mg/4 mL in single-dose vial) for the indications of breast cancer (BC), non-small cell lung cancer (NSCLC), castration-resistant prostate cancer (CRPC), gastric adenocarcinoma (GC), and squamous cell carcinoma of the head and neck (SCCHN). The listed drug (LD) is Taxotere (docetaxel) Injection (NDA 020449, initial US approval 1996). The indications and dosing regimen of the proposed drug product are the same as that of the LD.

The Applicant submitted the results from an open-label, randomized, single-dose, two-way crossover bioequivalence study (20-VIN-0225) that was conducted in 46 patients with solid tumors to compare the pharmacokinetics of the proposed product to the LD to support the approval. The bioequivalence between the test and LD products is based on the 90% confidence intervals (CIs) on area under the curve (AUC) and maximum plasma concentration (C_{max}) for total and free (unbound) and total docetaxel. The study results demonstrate bioequivalence between the proposed test and LD products for both total and free docetaxel (Table 2).

1.1 Recommendations

This NDA is approvable from a clinical pharmacology perspective.

Review Issues	Recommendations and Comments
Supportive evidence of effectiveness	Based on the scientific bridge established through a bioequivalence study between Beizray (docetaxel) Injection and Taxotere (docetaxel) Injection.
General dosing instructions	The proposed dosing regimen of this product is based on the approved recommended dosage for the LD product.
Dosing in patient subgroups (intrinsic and extrinsic factors)	The proposed dosing regimen of this product will be the same as that described for the LD product as adequate scientific bridge between Beizray and Taxotere has been established.
Bridge between the "to-be-marketed" and listed drug formulations	Bioequivalence between Beizray and Taxotere Injection was demonstrated.

1.2 Post-Marketing Requirements and Commitment

None.

2. SUMMARY OF CLINICAL PHARMACOLOGY ASSESSMENT

2.1 Pharmacology and Clinical Pharmacokinetics

Docetaxel is an antineoplastic agent belonging to the taxoid family. It acts by disrupting the microtubular network in cells that is essential for mitotic and interphase cellular functions. The following PK parameters for docetaxel are from the labeling of the Listed Drug, Taxotere (docetaxel) Injection.

Absorption: The pharmacokinetics of docetaxel were evaluated in patients with cancer after administration of 20 mg/m^2 to 115 mg/m^2. The area under the curve (AUC) was dose proportional following doses of 70 mg/m^2 to 115 mg/m^2 with infusion times of 1 to 2 hours. Docetaxel's pharmacokinetic profile is consistent with a three-compartment pharmacokinetic model, with initial rapid distribution phase and the late (terminal) phase.

Distribution: Mean steady state volume of distribution is 113 L. Docetaxel is approximately 94% protein bound in vitro, mainly to α1-acid glycoprotein, albumin, and lipoproteins. In three patients with cancer, the in vitro binding to plasma proteins was approximately 97%.

Metabolism: Docetaxel is metabolized by CYP3A4 in vitro (also see Drug Interaction and Therapeutic Individualization below).

Elimination: The estimated mean total body clearance is 18 L/h/m^2 (range of means: 14 to 23) and mean terminal elimination half-life is 116 hours (range of means: 92 to 135).

Excretion: In three patients with cancer, urinary and fecal excretion accounted for approximately 6% and 75% of the administered radioactivity, respectively, within 7 days. About 80% of the radioactivity recovered in feces was excreted during the first 48 hours as 1 major and 3 minor metabolites with less than 8% as unchanged drug.

Hepatic Impairment: Patients with mild to moderate liver impairment (AST and/or ALT >1.5 times ULN concomitant with alkaline phosphatase >2.5 times ULN), total body clearance was lowered by an average of 27%, resulting in a 38% increase in systemic exposure (AUC). Avoid TAXOTERE in patients with combined abnormalities of transaminase and alkaline phosphatase. Patients with severe hepatic impairment have not been studied.

Drug Interaction:

- Ketoconazole (strong CYP3A4 inhibitor): AUC of docetaxel was increased 2.2-fold and clearance was reduced by 49% when docetaxel was co-administered with ketoconazole.

- Dexamethasone: Docetaxel total body clearance was not modified by pretreatment with dexamethasone.

2.2 Dosing and Therapeutic Individualization

2.2.1 General dosing

For all indications, BEIZRAY is recommended to be administered IV over 1 hour every 3 weeks (Q3W) and the recommended dose for each indication is the same as that for the LD, as listed below:

Breast Cancer

• Locally advanced or metastatic: 60 mg/m^2 to 100 mg/m^2 monotherapy
• Adjuvant: 75 mg/m^2 with doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 Q3W.

Non-small Cell Lung Cancer

• After failure of prior platinum-based chemotherapy: 75 mg/m^2 monotherapy.
• Chemotherapy-naïve: 75 mg/m^2 followed by cisplatin 75 mg/m^2.

Prostate Cancer

• 75 mg/m^2 with 5 mg prednisone twice a day continuously.

Gastric Adenocarcinoma

• 75 mg/m^2 followed by cisplatin 75 mg/m^2 (both on day 1 only) followed by fluorouracil 750 mg/m^2/day as a 24-hr IV (days 1–5), starting at end of cisplatin infusion.

Head and Neck Cancer

- Induction Chemotherapy Followed by Radiotherapy: 75 mg/m^2 followed by cisplatin 75 mg/m^2 on day 1 followed by fluorouracil 750 mg/m^2/day for 5 days.
- Induction Chemotherapy Followed by Chemoradiotherapy: 75 mg/m^2 followed by cisplatin 100 mg/m^2 on day 1 followed fluorouracil 1000 mg/m^2/day for 4 days.

2.2.2 Therapeutic individualization

For all indications, toxicities may warrant dosage adjustments. The dosage modifications due to adverse reactions, hepatic impairments and the concomitant use of CYP3A4 Inhibitors are the same as that of the LD.

Hepatic Impairment: In case of AST/ALT >2.5 to ≤5 × ULN and AP ≤2.5 × ULN, or AST/ALT >1.5 to ≤5 × ULN and AP >2.5 to ≤5 × ULN, BEIZRAY should be reduced by 20%. In case of AST/ALT >5 × ULN and/or AP >5 × ULN, BEIZRAY should be stopped.

Concomitant Administration of Strong CYP3A4 Inhibitors: Avoid using concomitant strong CYP3A4 inhibitors. There are no clinical data with a dose adjustment in patients receiving strong CYP3A4 inhibitors. Based on extrapolation from a pharmacokinetic study, consider a 50% docetaxel dose reduction if patients require coadministration of a strong CYP3A4 inhibitor.

2.3 Outstanding Issues

No outstanding issues.

3. COMPREHENSIVE CLINICAL PHARMACOLOGY REVIEW

3.1 Overview of the Product and Regulatory Background

Taxotere (docetaxel) was originally approved on 05/14/1996 for the treatment of refractory, locally advanced or metastatic breast cancer under NDA 020449. Additional indications were approved including the treatment of advanced or metastatic non-small cell lung cancer after failure of platinum containing chemotherapy (Dec 1999), metastatic, hormone-refractory prostate cancer in combination with prednisone (May 2004), advanced gastric cancer in combination with cisplatin and fluorouracil (Mar 2006), and locally advanced, squamous cell head and neck cancer in combination with cisplatin and fluorouracil (Oct 2006). The originally approved Taxotere product (currently discontinued) was a two-vial formulation (Injection Concentrate and Diluent) available as 20 mg/0.5 mL and 80 mg/20 mL (40 mg/mL). The diluent contained 13% ethanol in water for injection. The current Taxotere product is available a one-vial formulation supplied as 20 mg/1 mL, 80 mg/4 mL and 160 mg/8 mL (20 mg/mL) in single-dose vials, which requires no prior dilution with diluent.

In the current NDA 218711, the Applicant is seeking approval for Beizray (BH009 [docetaxel] Injection, 20 mg/mL (80 mg/4 mL in single-dose vial) under the 505(b)(2) pathway referencing

Taxotere (docetaxel) Injection under NDA 020449. The proposed product, Beizray, has the same active moiety but contains different inactive ingredients and the Applicant is proposing the same dosing regimens and indications as that of the LD Taxotere. Docetaxel is highly lipophilic and practically insoluble in water. In Taxotere formulation, Polysorbate 80 is used as a (b) (4) (b) (4) Taxotere requires no prior dilution with diluent and is ready to add to infusion solution of either 0.9% sodium chloride or 5% dextrose solution. The proposed product Beizray does not contain (b) (4) Instead, it is co-packed with a single vial of 25% human albumin solution. Per the Applicant, human albumin is used (b) (4) (b) (4) The human albumin solution is added to infusion solution (0.9% Sodium Chloride (b) (4) prior to addition of Beizray solution.

To support the approval of this NDA, the Applicant conducted an open-label, randomized, single-dose, two-way crossover bioequivalence (BE) study comparing Beizray (docetaxel) Injection 20 mg/mL with Winthrop (docetaxel) Injection 20 mg/mL, an authorized generic drug of Taxotere in patients with solid tumors who will be receiving treatment with docetaxel monotherapy at a dose of 75 mg/m^2.

3.2 General Pharmacological and Pharmacokinetic Characteristics

Refer to Section 2.1.

3.3 Clinical Pharmacology Questions

3.3.1 Has a scientific bridge been established between drug product(s) used in the literature studies and the proposed drug product to support the acceptance of the scientific literature?

Yes. A scientific bridge has been established between Beizray (docetaxel) Injection and Taxotere (docetaxel LD) Injection.

The Applicant conducted a multi-center, open label, randomized, single-dose, two-way crossover bioequivalence study to compare the proposed product, Beizray (BH009 [docetaxel]) Injection 20 mg/mL with Winthrop (docetaxel) Injection 20 mg/mL, an authorized generic drug of Taxotere in patients with solid tumors who will be receiving treatment with docetaxel monotherapy at a dose of 75 mg/m^2.

Table 1: Design of Study 20-VIN-0225

Purpose	Establish bioequivalence of Beizray (docetaxel) Injection (test) against the approved Winthrop (docetaxel) Injection, an authorized generic drug of Taxotere in patients with solid tumors who will be receiving treatment with docetaxel monotherapy at a dose of 75 mg/m^2.
Study Design	Multicenter, open label, randomized, single-dose, two-way crossover. Washout period of at least 21 days between period 1 and period 2.
Study Population	Forty-six (46) subjects from 5 clinical sites were randomized into the study. Forty-one (41) subjects completed the study. Forty (40) were included in the statistical bioequivalence analysis.

	Site A: N = 16 Site B: N = 16 Site C: N = 4 Site D: N = 2 Site E: N = 2
Proposed Dose	A single dose Beizray (docetaxel) Injection 20 mg/mL (test) or Winthrop (docetaxel) Injection 20 mg/mL, administered as a 1-hour intravenous (IV) infusion on the first day of each study period.
Instruction for Concomitant Medication (DDI Potential)	All patients were premedicated with oral corticosteroids such as dexamethasone 16 mg per day for 3 days prior to docetaxel administration in order to reduce the incidence and severity of fluid retention and severity of hypersensitivity reactions. Antiemetics, i.e., prophylactic granisetron or ondansetron was given to all the patients before administration in both periods. Prophylactic dexamethasone and G-CSF were permitted at the discretion of the Investigator.
PK Sampling Schedule	Pre-dose, 30 minutes, 40 minutes and 50 minutes during infusion, 1.000 hour* (immediately at the actual end of infusion), and at 5 minutes, 10 minutes, 20 minutes, 30 minutes, 1, 2, 3, 6, 8, 12, 24 and 48 hours after the end of the docetaxel infusion in both study periods
ECG Monitoring Schedule	Screening, Day -1 in both study periods, and End-of-Study

Out of the 46 randomized patients, 4 were withdrawn from the study (Patients Randomization Nos. (b) (6) withdrew consent in period 1) and 1 patient withdrew from the study (Patient (b) (6) was withdrawn due to disease exacerbation/progression in period 1). 41 completed both periods of the study. Patient (b) (6) had pre-dose concentration of both total and free docetaxel >5% Cmax, thus was excluded from the statistical analysis. In summary, a total of 40 evaluable patients were included in the statistical analysis.

Per the pre-specified study protocol and statistical analysis plan, centers with less than 5 evaluable patients were pooled and treated as a separate center for data analysis. Thus, data from Sites C, D and E are pooled for the statistical bioequivalence analysis.

The 90% confidence intervals for the GMR for C_{max}, AUC_{last}, and $AUC_{0\text{-}inf}$ of both total and free docetaxel were within the acceptable BE limits of 80% to 125% when comparing Beizray to Winthrop (Table 2, Table 3). Docetaxel is highly protein bound in vitro. Both total and free docetaxel meeting BE limits indicates that the faction of unbound (f_u) in vivo was similar for the proposed test product and LD products.

The reviewer conducted an independent analysis on the submission. The results of the reviewer's analysis also meet BE acceptance criteria and are in agreement with the sponsor's analysis with slight difference on AUC_{last} and $AUC_{0\text{-}inf}$, likely due to different trapezoidal method and terminal phase selection.

Table 2: Geometric Mean Pharmacokinetic Parameters (Study 20-VIN-0225)

Analyte	Parameter (unit)	Beizray Injection 20 mg/mL (Test)				Winthrop Injection 20 mg/mL (Reference)				Ratio
		Mean	CV%	Min	Max	Mean	CV%	Min	Max	(T/R)
	AUC_{last} (h*ng/mL)	3,910	47	1,270	11,200	3,820	39	1,240	8,620	1.0

Analyte	Parameter (unit)	Beizray Injection 20 mg/mL (Test)				Winthrop Injection 20 mg/mL (Reference)				Ratio
		Mean	CV%	Min	Max	Mean	CV%	Min	Max	(T/R)
Total Docetaxel	$AUC_{0\text{-}inf}$ (h*ng/mL)	4,080	46	1,400	11,400	4,020	38	1,400	8,890	1.0
	C_{max} (ng/mL)	4,020	38	1,890	10,200	3,970	35	1,980	8,580	1.0
	T_{max} (hr)	0.833	.	0.5	1.1	1	.	0.7	1.1	0.8
	$T_{1/2}$ (hr)	9.25	50	1.7	25	10	39	3.8	21	0.9
Free Docetaxel	AUC_{last} (h*ng/mL)	785	41	362	1,910	816	33	356	1626	1.0
	$AUC_{0\text{-}inf}$ (h*ng/mL)	819	39	396	1,940	853	32	406	1,660	1.0
	C_{max} (ng/mL)	761	35	370	1,730	807	33	406	1,700	0.9
	T_{max} (hr)	0.833	.	0.5	1.0	1.0	.	0.5	2	0.8
	$T_{1/2}$ (hr)	15	32	7.6	25	17	21	7.5	24	0.9

Table 3: Summary Statistics for Bioequivalence Evaluation (Study 20-VIN-0225)

Analyte	Parameter (unit)	Beizray Injection 20 mg/mL (Test)	Winthrop Injection 20 mg/mL (Reference)	Ratio of Test / Reference	90% Confidence Interval of Ratio
Total Docetaxel	AUC_{last} (h*ng/mL)	3,590	3,590	1.0	92, 108
	$AUC_{0\text{-}\infty}$ (h*ng/mL)	3,760	3,800	1.0	92, 107
	C_{max} (ng/mL)	3,760	3,770	1.0	92, 108
Free Docetaxel	AUC_{last} (h*ng/mL)	750	775	1.0	90, 104
	$AUC_{0\text{-}\infty}$ (h*ng/mL)	784	814	1.0	90, 103
	Cmax (ng/mL)	721	774	0.9	85, 102

In conclusion, Study 20-VIN-0225 demonstrated that Beizray (docetaxel) Injection 20 mg/mL, is bioequivalent to Taxotere (docetaxel) Injection 20 mg/mL. The design of the study was reasonable for this evaluation (e.g., PK sampling, docetaxel dose, sample size). The reviewer conducted sensitivity analyses to confirm that observed protocol deviations did not affect the overall assessment. OSIS declined to conduct an inspection given that the site had been recently inspected (Refer to the OSIS inspection memorandum for more details).

4. APPENDICES

4.1 Bioanalytical Method

Total and Free (unbound) Docetaxel in human plasma were analyzed using Liquid-Liquid Extraction Method with Liquid Chromatography – Electro Spray Ionization – Mass

Spectrometry/ Mass Spectrometry (LC-ESIMS/MS). The assay validation parameters are as indicated in Table 4. The Office of Clinical Pharmacology review team has assessed the adequacy and acceptability of the following bioanalytical methods used in clinical studies and have determined that these methods are acceptable.

Table 4: Summary of method performance of the bioanalytical method to measure Total and Free Docetaxel in human plasma

Bioanalytical method validation report name, amendments, and hyperlinks	• Determination of Total Docetaxel in K_3EDTA Human Plasma by Using LC-ESI-MS/MS. Report No. VIN-BRD-MV-1415 • Determination of Free Docetaxel in K_3EDTA Human Plasma by Using LC-ESI-MS/MS. Report No. VIN-BRD-MV-1416	
Method description	Liquid-Liquid Extraction Method with Liquid Chromatography – Electro Spray Ionization – Mass Spectrometry/ Mass Spectrometry (LC-ESIMS/MS)	
Materials used for calibration curve & concentration	Biological matrix: K_3EDTA human plasma Internal standard: Docetaxel-d9 Total Docetaxel: 10.000, 20.000, 60.000, 120.000, 240.000, 600.000, 1200.000, 2400.000, 4800.000, 6000.000 ng/mL Free Docetaxel: 1.000, 2.000, 6.000, 12.000, 24.000, 60.000, 120.000, 240.000, 480.000, 600.000 ng/mL	
Validated assay range	Total Docetaxel: 10.000 ng/mL (LLOQ) to 6000.000 ng/mL (ULOQ) in human plasma Free Docetaxel: 1.000 ng/mL (LLOQ) to 600.000 ng/mL (ULOQ) in human plasma	
Material used for QCs & concentration	Biological matrix: K_3EDTA human plasma Total Docetaxel: 10.000 ng/mL (LLOQ QC), 30.000 ng/mL (LQC), 660.000 ng/mL (MQC2), 2250.000 ng/mL (MQC1), 4500.000 ng/mL (HQC) Free Docetaxel: 1.000 ng/mL (LLOQ QC), 66.000 ng/mL (MQC2), 225.000 ng/mL (MQC1), 450.000 ng/mL (HQC)	
Source & lot of reagents (LBA)	Docetaxel Batch: 100666-201704. Source: (b) (4) (b) (4) Expiration date: N/A	Docetaxel-d9 Batch no: 01-MAR-20-50 Source: (b) (4) Expiration date: 16Mar2023
Regression model & weighting	Regressions model: Linear regression Weighting factor: $1/x^2$	
Validation parameters	**Method validation summary: Total Docetaxel Report No. VIN-BRD-MV-1415**	
Standard calibration curve performance during accuracy & precision	Range of r2 values	0.9870 to 0.9989
	CC Standards except LLOQ	Precision (%CV): 3.41% to 5.93% % Mean Bias: -5.43% to 4.72%
	LLOQ Standard	Precision (%CV): 5% % Mean Bias: -1.18%
QCs performance during accuracy & precision	Cumulative accuracy (%bias) in QCs	Precision (%CV): 0.79% to 4.33% % Mean Bias: -0.63% to 11.07%
	Inter-batch %CV	Precision (%CV): 0.79% to 4.33% % Mean Bias: -0.63% to 11.07%
Selectivity & matrix effect	Biological Matrix	9 lots of human plasma spiked at the LLOQ; No interference noted; % Accuracy of LLOQ: 88.66% to 108.76%
	Biological Matrix in presence of Metabolite	6 lots of human plasma spiked at the LLOQ; ≤ 2.39% interference at the retention

		time of analyte at LLOQ; No interference at the retention time of ISTD; % Accuracy of LLOQ: 101.37% to 103.35%
Interference & specificity	Concomitant medication interference: (Acetaminophen, Caffeine, Cetirizine, Domperidone, Diclofenac, Ibuprofen, Nicotine, Ranitidine, Granisetron, Ondensetron, Dexamethason)	LQC: Precision (%CV): 1.95% % Mean Bias: 8.11% HQC: Precision (%CV): 1.68% % Mean Bias: 5.16%
Hemolysis effect	Hemolysis effect was analyzed as part of matrix effect and concomitant medication experiments. No suppression or enhancement noted in 5 out of 5 matrix lots.	
Lipemic effect	Lipemic effect was analyzed as part of matrix effect and concomitant medication experiments. No suppression or enhancement noted in 5 out of 5 matrix lots.	
Dilution linearity	27000.000 ng/mL with 10 x dilution	Precision (%CV): 5.44% % Mean Bias: 9.22%
Bench-top/process stability	Bench-top stability: 12 hours and 8 hours with and without metabolite, respectively at ambient temperature. Process stability: 118 hours at 5±3°C	
Freeze-Thaw stability	5 Cycles at freezing temperature of -20±5 °C and -78±8 °C	
Long-term storage	194 Days at -20±5 °C and -78±8 °C	
Carry over	% Carryover for Analyte: ≤ 6.73% % Carryover for ISTD: 0.00%	
Validation parameters	**Method validation summary: Free Docetaxel Report No. VIN-BRD-MV-1416**	
Standard calibration curve performance during accuracy & precision	Range of r^2 values	0.9917 to 0.9997
	CC Standards except LLOQ	Precision (%CV): 3.72% to 5.99% % Mean Bias: -2.37% to 1.60%
	LLOQ Standard	Precision (%CV): 5.72% % Mean Bias: -0.40%
QCs performance during accuracy & precision	Cumulative accuracy (%bias) in QCs	Precision (%CV): 2.77% to 8.70% % Mean Bias: -8.68% to 7.84%
	Inter-batch %CV	Precision (%CV): 0.63% to 3.16% % Mean Bias: -3.08% to 4.16%
Selectivity & matrix effect	Biological Matrix	9 lots of human plasma spiked at the LLOQ; ≤ 1.66% interference at the retention time of analyte at LLOQ; No interference at the retention time of ISTD; % Accuracy of LLOQ: 91.10% to 104%
Interference & specificity	Concomitant medication interference: (Granisetron, Ondensetron, Dexamethason)	LQC: Precision (%CV): 12.01% % Mean Bias: 5.23% HQC: Precision (%CV): 11.41% % Mean Bias: 0.06%
Hemolysis effect	Hemolysis effect was analyzed as part of matrix effect. No suppression or enhancement noted in 3 out of 3 matrix lots.	
Lipemic effect	Lipemic effect was analyzed as part of matrix effect. No suppression or enhancement noted in 3 out of 3 matrix lots.	
Dilution linearity	8000.000 ng/mL with 10 x dilution	Precision (%CV): 2.29% % Mean Bias: -0.39%

Bench-top/process stability	Bench-top stability: 14 hours at ambient temperature. Process stability: 99 hours at 5±3°C
Freeze-Thaw stability	5 Cycles at freezing temperature of -20±5 °C and -78±8 °C
Long-term storage	74 Days at -20±5 °C and 152 days at -78±8 °C
Carry over	% Carryover for Analyte: ≤ 5.26% % Carryover for ISTD: < 0.01%

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