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29 October 2025

RESPONSE TO PREA NON-COMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

Peter Kim, MD, MS
Director, Division of Anti-Infectives
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

NDA 209445
Sequence No. 0146
FETROJA® (cefiderocol) for Injection, 1 g/vial

Dear Dr. Kim:

Please refer to the "NOTIFICATION OF NON-COMPLIANCE WITH PREA" letter Shionogi received from the Agency on 14 October 2025. As discussed in greater detail below, Shionogi diligently completed the two required postmarketing pediatric clinical studies (PMRs) under the Pediatric Research Equity Act (PREA) (PMRs 3940-1 and 3940-2) and submitted the clinical study reports to the new drug application (NDA) for FETROJA (NDA 209445/S-002) in advance of the applicable deadlines. In doing so, Shionogi believed it complied with the requirements under PREA. The studies generated meaningful information on pediatric use in accordance with the goals of PREA, and were submitted to FDA in a timely manner. There remains only modest additional work to be completed in order to inform (b) (4)

In light of the circumstances, including Shionogi's good faith effort to comply with PREA and its timely completion and submission of the pediatric study reports, Shionogi respectfully requests that FDA reconsider its PREA non-compliance determination.

In the alternative, Shionogi requests that FDA grant a deferral extension until (b) (4), so that Shionogi may remedy any technical PREA non-compliance (b) (4) (b) (4).

I. Regulatory History

The NDA for FETROJA® (cefiderocol) for injection, 1 gram per vial, was initially approved on 14 Nov 2019 as an antibiotic therapy for patients 18 years of age or older who have limited or no alternative treatment options for the treatment of complicated urinary tract infections (cUTIs), including pyelonephritis caused by susceptible Gram-negative microorganisms. A supplemental NDA (sNDA) 002 was approved by the FDA on 25 Sep 2020, and FETROJA® is now indicated in patients 18 years of age or older for the treatment of the following infections caused by susceptible Gram-negative microorganisms: cUTIs, including pyelonephritis, and hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP).

FDA's approval of sNDA 002 identified the following required pediatric studies under PREA to evaluate the pharmacokinetics, safety and tolerability of FETROJA (cefiderocol): 3940-1 in children from 3 months to less than 18 years of age with cUTI and HABP/VABP (study APEKS-PEDI), and 3940-2 in children from birth to less than 3 months of age with suspected or confirmed Gram-negative infections (Study NEO-CEFI).

By letter dated May 10, 2024, FDA granted an extension of PMR 3940-1 until March 2025. By letter dated July 11, 2024, FDA granted an extension of PMR 3940-2 until January 2026.

Shionogi completed both studies and submitted final study reports for each as follows:

PMR under PREA	Pediatric Clinical Study	PREA Deadline	Final Study Report Submitted
3940-1	Conduct an open-label, randomized, multicenter, active-controlled trial to evaluate the pharmacokinetics, safety and tolerability of FETROJA (cefiderocol) in children from 3 months to less than 18 years of age with cUTI and HABP/VABP.	Final Report Submission March 2025 (deferral extension date)	26 March 2025 IND 116787 SN0397
3940-2	Conduct an open-label, single arm, non-comparative study to evaluate the pharmacokinetics, safety and tolerability of multiple doses of FETROJA (cefiderocol) in children from birth to less than 3 months of age with suspected or confirmed Gram-negative infections.	Final Report Submission January 2026 (deferral extension date)	18 September 2025 IND 116787 SN0403

By letter dated 7 October 2025, and received by Shionogi 14 October 2025, FDA issued a "NOTIFICATION OF NON-COMPLIANCE WITH PREA." The notification states: "…you have failed to meet the postmarketing requirement (PMR) of the Pediatric Research Equity Act (PREA) for this application because you have not yet submitted your pediatric assessment for the following: PMR 3940-1, which was deferred until March 31, 2025." The notification does not acknowledge that Shionogi did complete each study and submit to FDA final study reports before the applicable deadlines.

II. Discussion and Requested Action

As set forth above, Shionogi diligently conducted both of the required pediatric clinical studies for each PMR (3940-1 and 3940-2) (b) (4) further submitted the clinical study reports for each study to the NDA in a timely manner, with the report for PMR 3940-1 submitted on 26 March 2025, in advance of the 31 March 2025 deadline, and the report for PMR 3940-2 submitted on 18 September 2025, in advance of the [31] January 2026 deadline.

In completing the studies and submitting them to the NDA, Shionogi believed that it had complied with FDA's requirements under PREA. The statute provides that a sponsor submit a pediatric assessment "with the application," which Shionogi met when it submitted its pediatric assessments to the original NDA. *See* Federal Food, Drug and Cosmetic Act (FDCA) § 505(a)(1)(A). FDA's deferral extension granted to Shionogi similarly provided that the submission may be made "as part of your new drug application (NDA), **or** as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies.". Shionogi met this directive by submitting final study reports to the NDA for FETROJA.

Shionogi appreciates the importance of generating clinical information (b) (4) As such, Shionogi is conducting an analysis (b) (4) . Given the time required to complete these analyses, Shionogi is still in process on preparing a (b) (4) .

In light of the circumstances and the good faith efforts here, Shionogi respectfully requests that FDA reconsider its PREA non-compliance determination.

In the alternative, Shionogi requests a deferral extension until May 31, 2026 to allow for completing the outstanding analyses (b) (4) with PMR 3940-1.

This submission contains trade secret or confidential commercial information that is exempt from disclosure under 5 USC § 552(b)(4), 21 USC § 331(j), and 21 CFR § 20.61. Shionogi asks that FDA consult with Shionogi as provided in 21 CFR § 20.47 before making any part of this submission publicly available and that FDA preserve and protect the confidentiality of the information and data herein to the maximum extent permitted by law.

If there are any questions or comments regarding this submission, please contact me by phone at 862-505-0552 or by email at ann.wouters@shionogi.com.

Sincerely,

Ann Wouters, M.Sc.
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