U.S. Food and Drug Administrative

Center for Drug Evaluation and Research

Environmental Review

Bemotrizinol

June 5, 2026

Order ID:	OTC000039
Order Title:	Amending Over-the-Counter Monograph M020: Sunscreen Drug Products for Over-the-Counter Human Use, and Related Information
OTC Monograph:	M020
Active ingredients:	Bemotrizinol, at concentrations up to 6%

1. Executive Summary

FDA is issuing Final Administrative Order OTC000039, and, with this action, will amend the requirements for sunscreen drug products for over-the-counter (OTC) human use in Over-the-Counter Monograph M020: Sunscreen Drug Products for Over-the-Counter Human Use (OTC Monograph M020).[1] Final Administrative Order OTC000039 amends OTC Monograph M020 to add bemotrizinol (BEMT), at concentrations up to 6 percent, as a sunscreen active ingredient. On September 23, 2024, DSM Nutritional Products LLC (DSM or Requestor) submitted a Tier 1

[1] OTC Monograph M020 was initially set forth in Final Administrative Order OTC000006 Over-the-Counter Monograph M020: Sunscreen Drug Products for Over-the-Counter Human Use, available via the OTC Monographs@FDA portal at https://www.accessdata.fda.gov/scripts/cder/omuf/. On September 24, 2021, FDA issued Proposed Administrative Order OTC000008 Amending Over-the-Counter Monograph M020: Sunscreen Drug Products for Over-the-Counter Human Use, available via the OTC Monographs@FDA portal at https://www.accessdata.fda.gov/scripts/cder/omuf/. The final order contained in this document does not address Proposed Administrative Order OTC000008 which, if finalized, would amend and revise OTC Monograph M020 to establish certain new conditions under which nonprescription sunscreen drug products would be determined to be generally recognized as safe and effective (GRASE). If OTC000008 is finalized, all sunscreen drug products marketed under OTC Monograph M020, including products containing bemotrizinol as a sunscreen active ingredient, would be required to meet the conditions described in OTC Monograph M020, as amended by OTC000008.

OTC monograph order request (OMOR)[2] to add BEMT, at concentrations up to 6 percent,[3] to OTC Monograph M020 for use as a sunscreen active ingredient.

The National Environmental Policy Act of 1969 (NEPA) requires Federal agencies to assess the environmental impact of their actions. FDA is required under NEPA to consider the environmental effect of its major federal actions, which among other activities include the establishment or amendment of monographs describing the conditions of use under which OTC human drug products have been found to be GRASE. While certain classes of actions are categorically excluded under NEPA and, therefore, ordinarily do not require the preparation of an environmental assessment (EA) or an environmental impact statement (EIS), the addition of BEMT to OTC Monograph M020 is not categorically excluded because this action is expected to increase the use of BEMT, a new sunscreen active ingredient, and the screening-level expected introduction concentration (EIC) of BEMT in nationwide freshwater was estimated to be 1.10 to 7.63 µg/L (ppb), thus exceeding the categorical exclusion level of 1 ppb.[4] Thus, an EA is required to evaluate the potential adverse environmental effects from the use of BEMT as an active ingredient for use in sunscreens.

On September 23, 2024, the Requestor submitted an initial EA that evaluated the potential adverse environmental effects from the use of BEMT at concentrations up to 6 percent as an OTC sunscreen active ingredient, and on May 8, 2026, the Requestor submitted a final EA, which is a revision of the initial EA based on additional study results submitted by the Requestor and on feedback and recommendations from FDA. The CDER EA reviewers reviewed the initial EA and identified inadequacies, primarily in chronic toxicity data in benthic organisms and environmental fate data in the aquatic environment. These data were requested given BEMT's potential for high-volume use and thus the potential for high EIC values. BEMT also is frequently detected in aquatic environments of countries where BEMT has been marketed for many years. In consideration of the OMOR requesting the addition of BEMT to the OTC sunscreen monograph, CDER EA reviewers recommended additional assessment for environmental exposure, including upper-bound EICs and expected environmental concentrations (EECs) in U.S. regions with relatively high sunscreen use, and aquatic EECs of BEMT from direct wash-off during swimming and other in-water recreational activities. CDER EA reviewers and the Requestor engaged in extensive communications through meetings and multiple requests for information. The Requestor agreed to conduct additional studies including ecotoxicity tests of BEMT on two benthic organisms (freshwater ostracod *Heterocypris incongruens* and marine amphipod *Leptocheirus plumulosus*) and an environmental fate study following the Organisation for Economic Co-operation and Development (OECD) 308 guidance, and additional assessments. This additional information has been incorporated into a final EA, submitted on May 8, 2026. The final EA includes the additional study results submitted

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[2] An OTC monograph order request (OMOR) means a request for an order submitted under section 505G(b)(5) of the FD&C Act (see section 744L(7) of the FD&C Act (21 U.S.C. 379j-71(7)). A Tier 1 OMOR means any OMOR not determined to be a Tier 2 OMOR (see section 744L(8) of the FD&C Act (21 U.S.C. 379j-71(8)). An OMOR requesting the addition of an active ingredient to an OTC monograph is not categorized as a Tier 2 OMOR and is, therefore, a Tier 1 OMOR.

[3] For the purposes of OTC Monograph M020, FDA interprets a concentration up to 6 percent to mean up to and including 6 percent.

[4] See 21 CFR 25.31(b).

by the Requestor and the feedback and recommendations provided by CDER EA reviewers since the submission of the initial EA.

After careful review of the final EA, of all Requestor-submitted information, and additional CDER-supplied information, the CDER EA reviewers have determined, based on the entirety of this information, that the information is sufficient to enable the Agency to determine whether the issuance of Final Administrative Order OTC000039 may significantly affect the quality of the human environment.[5] The final EA, supplemented by the scientific review, is adequate for this action.[6] Based on the information reviewed by the Agency, CDER EA reviewers have concluded that the issuance of Final Administrative Order OTC000039 is not expected to have significant effects on the quality of the human environment. Accordingly, a Finding of No Significant Impact (FONSI) is recommended, and an EIS will not be prepared.[7]

2. Summary of the Final Environmental Assessment

2.1. Substance of Interest

The Requestor identified BEMT ($C_{38}H_{49}N_3O_5$, 627.81 g/mol, CAS number 187393-00-6) as the only substance of interest for the EA. BEMT is an organic active ingredient (as opposed to an inorganic ingredient such as zinc oxide and titanium dioxide) for use in sunscreens that has high photostability and a broad-spectrum coverage across UVB (280 to 320 nm) and UVA (320 to 400 nm) ranges.

No other substances were assessed in the EA, as the EA states that no structurally related substances (SRSs) represent more than 10% of the dose and that known impurities are present at very low levels (total impurities <2% w/w as per the U.S. Pharmacopeia [USP] monograph).

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[5] FDA generally requires the entity requesting a particular FDA action to make necessary corrections to its EA. 21 CFR 25.40(b). In this case, while the Requestor made various updates to its initial EA, in some areas the final EA was not corrected as requested by the Agency. Consequently, CDER included additional information in its review. See id.

[6] See 21 CFR 25.15(a).

[7] 21 CFR 25.15(b), 25.40, and 25.41.

2.2. Expected Introduction Concentrations and Expected Environmental Concentrations

The Requestor estimated the EICs and EECs of BEMT in the environment under: (1) the conventional down-the-drain pathway, in which BEMT enters the environment through wash-off (and other pathways such as laundry) followed by wastewater treatment; and (2) the direct release scenario, in which BEMT enters the aquatic environment through direct wash-off during swimming and other in-water recreational activities.

Down-the-Drain Scenario

For the estimated use of BEMT in the U.S., the EA provided an estimate of (b) (4) metric tons/year based on global production of BEMT ((b) (4) tons/yr) and U.S. market share for sunscreens (26%), a projected "realistic" estimate of (b) (4) metric tons/year by 2037 based on a 4% annual growth rate, and a "conservative" (worst case or bounding) estimate of (b) (4) metric tons/year. Based on the latter two amounts, the Requestor calculated the EICs of BEMT in freshwater using the EIC calculation described in the FDA 1998 guidance [1] and then refined the results by using a model to predict the removal of BEMT by wastewater treatment plants (WWTPs) (EA Appendix 4). The partition of BEMT in WWTP effluent and sludge, predicted by the U.S. Environmental Protection Agency (EPA) Sewage Treatment Plant (STP) Fugacity Model v4.11, is 9.66% and 89.58%, respectively. The Requestor also applied dilution factors of 10 and 100 to the refined EICs to derive the aquatic EECs for freshwater and coastal marine water, respectively.

To assess the upper-bound environmental exposures of BEMT, the Requestor estimated the EICs and EECs in the south and west regions of the U.S., where sunscreen use is relatively higher than in other regions. This estimate followed a similar approach as deriving the national EICs and EECs. Differences in the regional EICs and EECs result from the regional data for calculation, including market share data on sunscreen sales by U.S. region over the past three years, and WWTP treated wastewater volumes and biosolids amounts in these regions. Results of the down-the-drain scenario are summarized in Table 1 below.

Based on the EECs in freshwater and marine water, the Requestor estimated the EECs of BEMT in freshly deposited sediment following the European Medicines Agency (EMA) 2024 guideline [2]. The Requestor used the adsorption coefficient (K_d) of BEMT in soil, rather than K_{OC}, for EEC-sediment estimation, as no statistically significant correlation was observed between K_d and soil organic carbon content (OC%) (Kendall's tau 0.2, p-value >0.05).

As to the terrestrial environment, the Requestor first calculated the EICs in biosolids using the estimated national and regional use data, national and regional biosolids generation amounts, and the predicted proportion of BEMT binding to WWTP sludge (89.58%), and subsequently calculated the national and regional EICs in soil following the EMA 2024 guideline [2] and using the highest biosolids application rate of 100 tons/acre (i.e., 22.4 kg/m^2) in the U.S. [3].

Table 1. Expected Introduction Concentrations and Expected Environmental Concentrations for the Down-the-Drain Scenario

Compartment	Region	Realistic Scenario ((b) (4) Tons/Year)		Conservative Scenario ((b) (4) Tons/Year)	
		EIC	EEC	EIC	EEC
Freshwater	National	Refined: 1.10 ppb	0.110 ppb	Refined: 7.63 ppb	0.763 ppb
	South region	Refined: 1.41 ppb	0.141 ppb	Refined: 9.77 ppb	0.977 ppb
	West region	Refined: 1.31 ppb	0.131 ppb	Refined: 9.07 ppb	0.907 ppb
Freshwater sediment	National		3.57 mg/kg dw		24.76 mg/kg dw
	South region		4.57 mg/kg dw		31.71 mg/kg dw
	West region		4.25 mg/kg dw		29.43 mg/kg dw
Marine water	National		0.011 ppb		0.0763 ppb
	South region		0.014 ppb		0.0977 ppb
	West region		0.013 ppb		0.0907 ppb
Marine sediment	National		0.36 mg/kg dw		2.47 mg/kg dw
	South region		0.46 mg/kg dw		3.17 mg/kg dw
	West region		0.42 mg/kg dw		2.94 mg/kg dw
Soil	National	4.88 mg/kg dw	21.8 mg/kg dw*	33.8 mg/kg dw	151 mg/kg dw*
	South region	6.89 mg/kg dw	30.8 mg/kg dw*	47.7 mg/kg dw	214 mg/kg dw*
	West region	6.71 mg/kg dw	30.0 mg/kg dw*	46.5 mg/kg dw	208 mg/kg dw*

Source: Data from the Requestor's final Environmental Assessment
*Incorrect values. The Requestor had responded to a CDER request for further information, and agreed that the EECs should be equal to or less than the EIC as a conservative, worst-case assumption representing no depletion in soil. However, the Requestor did not update the EA with agreed-upon EEC values. As contemplated by 21 CFR 25.40(b), which indicates FDA may include additional information when necessary, CDER used the adjusted EECs in the review. See Section 3 of this review for more information.
Abbreviations: dw, dry weight; ppb, µg/L.

Direct Release Scenario

As to this other release pathway for BEMT, in which BEMT enters the aquatic environment through direct wash-off during swimming and other in-water recreational activities, the Requestor estimated the EICs and EECs of BEMT in freshwater and marine coastal environments, and also summarized the literature-reported maximum measured environmental concentrations (MECs) of BEMT in countries/regions where BEMT has been marketed for years. The results from the EA are shown in Table 2 below.

Table 2. Expected Introduction Concentrations and Expected Environmental Concentrations for the Direct Release Scenario and Measured Environmental Concentrations

Compartment	EIC (1 Day)	Long-term EEC (91 Days)	Maximum MEC
Freshwater	0.047 ppb	4.15 ppb	4.28 ppb
Freshwater sediment	1.53 mg/kg dw	138.92 mg/kg dw	0.12 mg/kg dw
Marine water	0.103 ppb	0.0365 ppb	0.01 ppb
Marine sediment	0.33 mg/kg dw*	30.33 mg/kg dw*	0.085 mg/kg dw

Source: Data from the Requestor's final Environmental Assessment
*The CDER EA reviewers disagree. See Section 3 of this review for more information.
Abbreviations: dw, dry weight; ppb, µg/L.

Under the direct release scenario, the Requestor estimated the EIC of BEMT in freshwater and marine water following the European Chemicals Agency Emission Scenario Document for Product Type 19 (PT19) [4], based on some conservative assumptions such as the high-end number of swimmers (i.e., 687 swimmers per day for freshwater or 1,500 swimmers per day for marine coastal water for a given volume of water body 435,000 m^3). The aqueous EIC estimation also accounted for adsorption of BEMT to suspended matter in water, consistent with the EMA 2024 guideline [2]. Based on the aqueous EICs, the Requestor estimated the EICs in sediments using a similar approach as described above in the down-the-drain scenario (EA Appendix 7).

The Requestor derived long-term EECs in freshwater and corresponding sediment following the same PT19 guidance [4], based on emissions occurring over a 91-day period (one quarter of a year) to reflect continuous high-end sunscreen use during the swimming season, which represents a highly conservative seasonal use scenario. The Requestor estimated the long-term EEC of BEMT in marine water by accounting for tidal effects. Based on their estimates, 26.2% of BEMT is retained in marine water after regular daily tidal activity. Therefore, unlike EEC-freshwater, the EEC-marine water is significantly lower than the EIC-marine water, whereas the EEC-marine sediment still reflects the long-term accumulation of daily input.

2.3. Physicochemical Properties and Environmental Fate

The physicochemical data for BEMT submitted by the Requestor are summarized in Table 3 below.

Table 3. Physiochemical Data for BEMT Submitted by the Requestor

Physicochemical Parameter	Method	Results
Water solubility	OECD 105 (20 °C)	<0.014 ppm
	OECD 105 (25 °C)	4.5 ng/L
Dissociation constant (pK_a)	Hammett correlation method in ECHA 2024	-3 (triazin) and 9.4 (phenol)
Octanol/water partition coefficient ($logK_{OW}$)	OECD 107 and 117 (20 °C)	>5.7
Organic carbon-water partition coefficient ($logK_{OC}$)	OECD 106 (20 °C)	5.7–6.8 L/kg in soil
Vapor pressure	OECD 104 (25 °C)	5.9E-20 Pa

Source: Data provided by Requestor.
Abbreviations: ppm, mg/L.

These data indicate that BEMT has very low water solubility, does not dissociate or protonate at environmentally relevant pH (5 to 8), exhibits high hydrophobicity and high binding capacity to organic matter in soils and sediments, and is not volatilized.

In addition, the Requestor submitted environmental fate data for BEMT as summarized in Table 4 below.

Table 4. Environmental Fate Data for BEMT Submitted by the Requestor

Environ. Fate Study	Method	Results
Forced degradation study	Internal Standard Operating Procedure	Insignificant mass balance loss and degradation of BEMT (<5% w/w) in any of the stress conditions*
Ready biodegradability in activated sludge	OECD 301F (28 days)	Biodegradation: ca. 3%; not readily biodegradable
Aerobic transformation in soil	OECD 307 (120 days)	102–112% of nominally applied BEMT was recovered at day 120; DT_{50} >1,000 days
Aerobic transformation in aquatic sediment systems	OECD 308 (4 weeks)	The study was deemed technically not feasible; no reliable quantitative data
WWTP removal	U.S. EPA STP Fugacity Model v4.11	Biodegradation: 0.76%; Adsorption to sludge: 89.58%; Effluent: 9.66%
Bioaccumulation in fish (carp *C. carpio*)	MITI guideline (56 days)	For exposure conc. of 0.1 ppm and 1.0 ppm, BCF <19 and <3, respectively

Source: Data provided by Requestor.
*The test stress conditions included: (1) Thermal (heat) at 80 °C; (2) Humidity at 80 °C and 75% relative humidity; (3) Acid at room temperature and at 60 °C with 0.1 M HCl; (4) Base: at room temperature and at 60 °C with 0.1 M NaOH; (5) Oxidation: at room temperature with 1% H_2O_2; and (6) Photostability: at room temperature exposed to > 1.2 MLux*h / 200 W*h/m^2.
Abbreviations: ppm, mg/L.

The forced degradation study, OECD 301F, and OECD 307 test results demonstrate that BEMT is highly resistant to degradation under a range of environmental conditions, even under extreme stress. No degradation products were identified under forced degradation conditions. This stability rules out significant degradation or transformation of BEMT in the tested environments,

suggesting that BEMT could be highly persistent without substantial breakdown in typical environmental settings.

Following the CDER EA reviewers' recommendation, the Requestor conducted a study following the OECD 308 guidelines with some modifications (OECD 308 study) to investigate the fate of BEMT, particularly the formation of non-extractable residues (NER), in water-sediment systems. The study was conducted under non-GLP conditions using non-radiolabeled BEMT. Results qualitatively indicated a rapid transfer of BEMT from the water phase to sediment shortly after application. Nevertheless, the Requestor could not quantify BEMT reliably in water or sediment samples mainly due to unresolved analytical issues and unexpected contamination of background sediment samples. As a result, the OECD 308 study yielded no quantitative data on NER, degradation kinetics, or dissipation rates of BEMT in water-sediment systems. Therefore, the results should be viewed as preliminary and informative. See Section 3 of this review for more information.

Based on model prediction, approximately 89% of BEMT is expected to partition to sludge during wastewater treatment, with ~10% remaining in the final effluent. Biodegradation of BEMT in WWTPs is predicted to be negligible, <1%.

Significant bioaccumulation of BEMT in aquatic organisms is not expected. The bioaccumulation study indicated that BEMT has low potential for bioaccumulation in fish. The Requestor's literature review also showed low bioaccumulation of BEMT in sediment-dwelling worm *Hediste diversicolor*.

Overall, the Requestor concluded that BEMT's environmental fate is characterized by high stability and strong adsorption properties, resulting in limited mobility and low bioavailability in both aquatic and soil environments. BEMT released into the aquatic environment rapidly partitions from the aqueous phase to particulate matter and sediments. When released into the terrestrial environment, such as through the application of biosolids to land, BEMT will predominantly remain in soil, while evaporation to air or migration to groundwater is expected to be negligible.

2.4. Environmental Effects

The Requestor provided ecotoxicity data for BEMT in relevant aquatic and terrestrial organisms, including microbes in activated sludge, freshwater organisms (algae, daphnia, and fish), benthic organisms (freshwater ostracod and marine amphipod), and terrestrial organisms (soil microbes and earthworm). Results including no observed effect concentrations (NOECs), the lowest effect concentrations (LOECs), and effect concentrations (ECs), are summarized in Table 5 below.

Table 5. Ecotoxicity Data for BEMT Submitted by the Requestor

Organism	Method	Duration	Endpoint	Results
Microbes in activated sludge	OECD 209	3 hours	Respiration inhibition	NOEC ≥1,000 ppm
Green algae (*D. subspicatus*)	OECD 201	72 hours	Growth inhibition	NOEC ≥100 ppm (17 ppb)*
Aquatic invertebrate (*D. magna*)	OECD 202	Acute, 48 hours	Mobility	NOEC ≥100 ppm (0.114 ppm)*
Aquatic invertebrate (*D. magna*)	OECD 211	Chronic, 21 days	Mortality, growth, reproduction	NOEC ≥1.0 ppm (0.7 ppm)*
Japanese medaka (*O. latipes*)	Institute of Ecotoxicology 1999	Acute, 48 hours	Mortality	NOEC ≥205 ppm
Zebrafish (*D. rerio*)	OECD 203	Acute, 96 hours	Mortality	NOEC ≥100 ppm (0.81 ppb)*
Fish	iSafeRat fishEC10 v2.0	Chronic	Growth inhibition	No toxic effect was identified; the model predicted 32-day EC_{10} of BEMT surpasses its water solubility
Freshwater ostracod (*H. incongruens*)	Modified ISO 14371 (2012) and Niyommaneerat et al. 2017 [5]	31 days; BEMT exposure for 14 days (survival and growth); followed by incubation w/o BEMT (reproduction)	Survival, growth, and reproduction	NOEC = 505 mg/kg dw** LOEC = 1,010 mg/kg dw**
Marine amphipod (*L plumulosus*)	U.S. EPA methods (600/R-01/020, 600/R-94/025)	28 days	Survival, growth, and reproduction	NOEC ≥1,000 mg/kg dw
Soil microbes	OECD 216	28 days	Inhibition of nitrogen transformation	NOEC ≥1,000 mg/kg dw
Earthworm (*E. fetida*)	OECD 222	28 days	Survival, growth, and reproduction	NOEC ≥1,000 mg/kg dw

Source: Data provided by Requestor.
*Nominal concentration and measured concentration (in parentheses). The measured concentration of BEMT in the filtrate of supersaturated solution was lower than the nominal concentration due to the low water solubility.
**The CDER EA reviewers disagree. See Section 3 of this review for more information.
Abbreviations: dw, dry weight; ppb, µg/L; ppm, mg/L.

The freshwater ostracod study is the only one showing toxic effects of BEMT, specifically growth inhibition and reduced reproduction (see Table 6 below).

Table 6. Freshwater Ostracod Toxicity Results for BEMT Submitted by the Requestor

Endpoint	Statistical NOEC	Statistical LOEC	Interpretation NOEC	Interpretation LOEC	Remark
Mortality (14 days)	-	-			LC50-14d > 1010 mg/kg
Length (14 days)	505	1010	505	1010	-
Egg-laying ratio	505	1010	505	1010	-
Life span	126	505	505	1010	-
First day of brooding	126	505	1010	n/a	-
Mean day of egg production	126	505	1010	n/a	-
Total number of eggs produced	126	505	505	1010	-
Mean lifetime egg production	126	505	505	1010	-
Hatching ratio	505	n/a	505	n/a	-
Reproductive rate	n/a	126	n/a	n/a	-

Source: Data provided by Requestor.

The Requestor assessed and identified NOECs and LOECs by integrating statistical outcomes with biological relevance and endpoint-specific considerations. While statistically identified NOECs were observed at lower exposure levels for several reproductive endpoints, the Requestor derived an overall NOEC at 505 mg/kg. This conclusion was caveated in EA Appendix 11 by clarifying that this value should be considered as supportive rather than definitive given the uncertainty linked to the ostracod performance in this study and the unknown impact of the preparation of the sediment. More specifically, the Requestor listed some problems in their ostracod study including different evaporation times between control and treatment groups, the thin and sticky film observed at the two highest dose groups, the decreased performance of the negative control compared to the proposed criteria in Niyommaneerat et al. (2017) [5], the solvent's unexpected impacts on the tested species, and potential effects from technician experience. Overall, the Requestor concluded that the NOEC of BEMT in sediment is 505 mg/kg dw and then normalized it to 12,625 mg/kg dw following the EMA 2024 guideline [2], based on the measured OC% of the sediment (0.4%) (The CDER EA reviewers disagree; see Section 3 of this review for more information).

No acute or chronic ecotoxicity of BEMT was observed in other aquatic and terrestrial organisms in the submitted studies, even at concentrations exceeding the solubility limit. The bioaccumulation study with carp (*Cyprinus carpio*), which was not specifically designed for chronic toxicity assessment, provided evidence of no adverse effects on fish over 56 days of exposure, even at a nominal exposure concentration of 1.0 ppm. Additionally, the Requestor's literature review identified no significant adverse effects of BEMT on zebrafish (*Danio rerio*) eggs, the sediment-dwelling worm *H. diversicolor*, or marine organisms including sea urchin, coral, microalga, and brine shrimp.

The Requestor provided a discussion on the low bioavailability of BEMT and its difficulty in passing through cell membranes due to its physicochemical properties such as large molecular mass. They also discussed animal test results showing the minimal absorption and bioaccumulation of BEMT in rats, fish, and soil/sediment-dwelling organisms.

2.5. Environmental Risk Assessment

For freshwater, marine water, and soil compartments, the Requestor stated that it was not possible to derive quantitative toxicity data (e.g., NOEC) since no toxicity was observed in any of the acute or chronic studies. Therefore, the Requestor performed a qualitative risk assessment by comparing the maximum EEC (e.g., data from the South region) to the highest tested concentration in the toxicity assays for each environmental compartment. The maximum EECs are 21-fold to several orders of magnitude lower than the highest tested concentrations, at which no adverse effects were observed, indicating that BEMT does not pose an unreasonable risk to water or soil compartment.

For sediment, the Requestor derived a predicted no-effect concentration (PNEC) for BEMT in sediment by applying an assessment factor (AF) to the normalized NOEC of 12,625 mg/kg dw from the ostracod study. An AF value of 50 was used in accordance with the EMA 2024 guideline [2], based on the availability of two chronic studies with sediment-dwelling organisms, i.e., freshwater ostracod and marine amphipod, representing different ecological niches and exposure pathways. The resulting PNEC in sediment is 252.5 mg/kg dw. The Requestor stated that this PNEC represents a conservative, worst-case risk characterization due to the substantial uncertainty associated with the validity and reliability of the ostracod study.

The Requestor calculated the risk quotient (RQ) as the ratio of maximum EEC to PNEC. The submitted RQs are summarized in Table 7 below.

Table 7. Risk Quotient Results for BEMT Submitted by the Requestor

Compartment	RQ_Down-the-Drain Scenario		RQ_Direct Release Scenario
	Realistic ((b) (4) Tons/Year)	Conservative ((b) (4) Tons/Year)	
Freshwater	<1*	<1*	0.000415
Freshwater sediment	0.0181	0.1255	0.55**
Marine water	<1*	<1*	0.0000365
Marine sediment	0.0018	0.0125	0.12**

Source: Data provided by Requestor.
*No toxicity was observed in these studies, and thus RQs were not calculated.
**The CDER EA reviewers disagree. See Section 3 of this review for more information.

The Requestor stated that all RQs were <1 for all compartments, indicating no environmental risk even under the highly conservative exposure assumptions applied in the direct release scenario. Consequently, the Requestor determined that no further risk refinement is needed. The Requestor emphasized that the EECs and associated RQs for the direct release scenario were derived using conservative exposure assumptions, including continuous daily use over a 91-day seasonal period, representing a high-end use scenario. This approach assumes maximum application rates and uninterrupted use during the peak season and therefore is expected to significantly overestimate actual environmental exposure, resulting in worst-case EEC and RQ estimates.

In conclusion, the Requestor stated that based on a comprehensive weight-of-evidence evaluation integrating environmental fate, exposure, bioavailability, and ecotoxicological effects, the proposed use of BEMT at concentrations up to 6% in OTC sunscreen drug products is not expected to result in significant adverse effects on the quality of the human environment. All risk characterizations, including worst-case exposure scenarios, demonstrate adequate margins of safety.

3. CDER Review

The main objectives of this FDA environmental review are to determine whether: (1) the EA contains sufficient information to enable the Agency to determine whether the proposed action may significantly affect the quality of the human environment; (2) the EA is accurate and objective; and (3) the proposed action may significantly affect the quality of the human environment.[8] FDA's review was conducted under the expertise of CDER's EA reviewers. The review of the final EA is as follows.

- The Requestor described the sunscreen active ingredient BEMT as the substance of interest for this EA, noting that SRSs and impurities are present at relatively low levels. This is consistent with the recommendations in the FDA 1998 guidance [1], which notes that an EA should focus on the active moiety and the predominant SRSs expected to enter or exist in the environment.[9]

[8] See 21 CFR 25.15 and 25.40.

[9] CDER acknowledges that the 1998 guidance [1] provides recommendations on how to prepare an EA for submission of drug and biologics applications. CDER is applying the same principles as expressed there to this request for agency action on an OMOR.

CDER EA reviewers reviewed the Requestor's "realistic" and "conservative" estimates for the use of BEMT in the U.S. and notes that the realistic estimate, (b) (4) tons/yr, was estimated for the year 2037 based on the global production (which does not include production in the U.S.) of (b) (4) tons/yr of BEMT in 2023, the U.S market share of current sunscreens of 26%, and an expected 4% annual growth rate. The starting amount during initial years, however, would likely be higher than the Requestor's estimated (b) (4) tons/yr, per Section 2.2 of this review, given that the global production amount would be higher after adding the initial U.S. amount (i.e., the 26% market share applied to the sum of the current (b) (4) tons/yr and initial U.S. amount). Nevertheless, based on the five-year projection estimate recommended in the FDA 1998 guidance [1], (b) (4) tons/yr amount could reasonably reflect the five-year time range, or longer, after BEMT enters the U.S. market. According to CDER EA reviewers' most recent analysis of the sunscreen consumption data in the U.S. [6], the 2016 consumption of the six most popular sunscreen active ingredients in the U.S.—which is expected to be adequately similar to today for purposes of this assessment—range from 4,780 to 35,100 tons/yr. Given BEMT is a frequently used sunscreen active ingredient in Europe, it is reasonable to expect that consumption of BEMT will be comparable to the existing popular sunscreen active ingredients in the U.S. The reviewers also expect that the tons per year will gradually increase once BEMT in sunscreens becomes familiar to consumers. However, a precise estimate by 2037 cannot be made. Therefore, the estimate of (b) (4) tons/year in the U.S. is acceptable for a conservative estimate given that the global market for BEMT in 2023 is (b) (4) tons/year. The conservative estimate of (b) (4) tons/yr for BEMT is close to the low-end of the above consumption range for existing popular sunscreen active ingredients that have been on the market for years and, for purposes of this review, this estimate is used to reflect the eventual long-term use of BEMT in the U.S.

- The majority of the estimated EICs and EECs of BEMT in the aquatic and terrestrial environments in the EA are adequate. The Requestor applied refinement approaches to the EICs in freshwater under both scenarios: model-predicted WWTP removal under the down-the-drain scenario, and adsorption of the substance to suspended matter in water under the direct release scenario. CDER considers these refinements and downstream estimates of EICs and EECs in water, sediment, and soil to be adequate, with the following exceptions:

    - The EECs in soil, i.e., the Requestor agreed to adopt the EICs as the EECs as a conservative, worst-case assumption representing no depletion in soil, but did not update the final EA with the agreed-upon EECs; the CDER EA reviewers nevertheless used the EICs as the EECs; and

    - The EIC and EEC in marine sediment under the direct release scenario, i.e., the CDER EA reviewers re-estimated the EIC-marine sediment (1 d) to be 0.87 mg/kg dw and the long-term EEC-marine sediment (91 d) to be 79.2 mg/kg dw, accounting for tidal dilution and using a similar approach as described by the Requestor in the down-the-drain scenario (Section 2.2 above).

Under the direct release scenario, the CDER EA reviewers agree with the Requestor that the assumptions for EIC and EEC estimates were conservative. For example, the Requestor's high-end numbers of swimmers (i.e., 687 swimmers per day for freshwater and 1,500 swimmers per day for marine coastal water for a given volume of water body 435,000 m^3) are higher than the CDER EA reviewers' analysis of Virgin Islands Trunk Bay (geometric mean of 667 daily visitors[10] in 2025 for a central tendency water volume of 404,926 m^3). The CDER EA reviewers note that the estimated long-term EECs of BEMT in freshwater and marine water are close to the maximum MECs that the Requestor noted in the literature, suggesting that these estimated EECs are reasonable. CDER found higher MECs of BEMT in sea coastal water in a study by Gandar et al., 2025 [7], which reported concentrations of BEMT ranging from approximately 3 ppb at the end of the summer to 14 ppb in July in the Northwestern Mediterranean region of the Vermeille Coast, a popular tourist destination in summer. Nevertheless, these results reported by Gandar et al. should be considered cautiously because they used an in situ passive sampler to accumulate the analytes over the sampling period (18 days) directly in ambient seawater, and CDER notes that these reported concentrations of BEMT in coastal water (3 to 14 ppb) exceeded its water solubility (4.5 ng/L), indicating potential accumulation of undissolved BEMT on the passive sampler during the sampling period. The CDER EA reviewers also note that the estimated long-term EECs in sediments are two to three orders of magnitude higher than the reported maximum MECs (e.g., Fagervold et al., 2019 [8]), suggesting that depletion mechanisms, such as formation of NER of BEMT in sediments that could not be predicted by existing models, may exist in the real environment (discussed below).

- The CDER EA reviewers find that the EA's physicochemical data and environmental fate data for BEMT are adequate. Based on the submitted information, the CDER EA reviewers agree with the Requestor that BEMT is expected to be stable and persistent in the environment especially in soil and sediment, due to its strong adsorption to natural organic matter. The submitted OECD 308 study showed that BEMT rapidly partitioned from water phase to sediment, as expected, after being introduced to the water-sediment systems, with <50% remaining in water phase after 3-day incubation, <5% in water phase after 14-day incubation, and not detected in water phase after 20 days. Despite the study failing to reliably quantify BEMT in sediment (since non-radiolabeled BEMT was used for the test), the CDER EA reviewers note a decrease in measurable BEMT in the total water-sediment test systems after 14 days of incubation, suggesting potential formation of NER in sediment. This aligns with the CDER EA reviewers' hypothesis that other depletion mechanisms may exist, discussed above as part of our comparison of the estimated EECs with reported MECs of BEMT in sediments. The formation of NER in sediment would substantially decrease the bioavailable fraction of BEMT to benthic organisms, thereby reducing environmental exposure and mitigating ecological risks in aquatic ecosystems.

[10] Virgin Islands National Park Reports, https://irma.nps.gov/Stats/Reports/Park/VIIS; see "YTD Report".

- The CDER EA reviewers find that the ecotoxicity data submitted by the Requestor, as well as their literature review and discussion of environmental effects of BEMT, are adequate except for the overall NOEC in sediment from the ostracod study. Considering that the ostracod study is the only study showing toxic effects of BEMT, and that the potential effects of BEMT on benthic organisms are of concern because sediment serves as a major sink for BEMT in aquatic environments, the CDER EA reviewers considered the ostracod study results useful for a conservative risk assessment, notwithstanding the Requestor's statement that "given the number of uncertainties surrounding the relevance and reliability of the study, the results should not be used for further assessment." While CDER EA reviewers agree with some of DSM's concerns, the results of the study are still informative and provide some valuable information to supplement the NOEC and PNEC. Thus, CDER conducted an independent statistical analysis of the submitted ostracod study data. The results of CDER's analysis indicated an overall NOEC of 126 mg/kg dw and LOEC of 505 mg/kg dw. Specifically, CDER's statistical analysis notes some issues in the Requestor's implementation of the Williams test and Shirley-Williams test, and some test statistics were incorrectly computed. According to CDER's analysis, statistically significant changes were observed at 505 mg/kg dw for five endpoints (mortality, egg-laying ratio, life span, first day of brooding, and mean day of egg production). Despite reductions in hatching ratio and reproductive rate being observed at 126 mg/kg dw in CDER's statistical analysis, the CDER EA reviewers concur with the Requestor that these two endpoints can be excluded for assessment due to high data variability with coefficient variations over 20% (56 to 139%). CDER's statistical analysis report concluded that further evaluation is needed to determine if the statistically significant results are biologically significant to make a final determination of the NOEC and LOEC, and thus the CDER EA reviewers adopted the statistically supported NOEC of 126 mg/kg dw for a conservative risk assessment (see below). In addition, based on the totality of submitted ecotoxicity data, the CDER EA reviewers agree with the Requestor that BEMT has low toxicity to other aquatic and terrestrial organisms. While chronic toxicity data of BEMT to terrestrial plants were not provided, the CDER EA reviewers believe that this data is not needed for this EA considering the low bioavailability of BEMT for plant uptake and low toxicity observed in other terrestrial organisms.

- The environmental risk assessments of BEMT in aquatic and terrestrial environments are acceptable with the exception of certain calculations described below. While the CDER RQs calculated for sediments under the direct release scenario exceed the threshold of 1, for the reasons explained below, the CDER EA reviewers believe the environmental effects of BEMT will not be significant. The CDER EA reviewers agree that it may not be feasible to derive a conventional PNEC for BEMT in water or soil as no toxic effects were observed in the ecotoxicity tests. For sediment, CDER derived a new PNEC of 63 mg/kg dw based on the NOEC of 126 mg/kg dw per above, using the same approach used by the Requestor as discussed above in Section 2.5. Using this new PNEC, the CDER EA reviewers recalculated the RQ in freshwater sediment to be 2.2 (138.92 mg/kg dw / 63 mg/kg dw), and the RQ in marine sediment to be 1.3 (79.2 mg/kg dw / 63 mg/kg dw), exceeding the threshold of 1, indicating potential risks of BEMT to benthic organisms in sediments. Nevertheless, considering the conservative estimates of the long-term EECs in sediments (e.g., continuous high-end sunscreen use over a 91-day period during the swimming season), the likely formation of NER in sediment, the lack of documented significant impact in countries/regions where BEMT has been marketed for many years [7], and the CDER EA reviewers' conservatively adopted PNEC value (as discussed above regarding the use of the lower NOEC and LOEC), the potential long-term risks of BEMT to sediment-dwelling organisms are not expected to be significant. Overall, the CDER EA reviewers conclude that BEMT does not appear to cause significant adverse environmental effects in the aquatic and terrestrial environments at the expected levels of exposure.

4. Overall Assessment and Recommendation

Overall, the information submitted by the Requestor for BEMT, when considered together with the information reviewed by the CDER EA reviewers, is sufficient to enable CDER to determine whether the issuance of Final Administrative Order OTC000039 may significantly affect the quality of the human environment. The CDER EA reviewers find the EA, supplemented by the scientific review, to be adequate for this action.

Based on the information available to date, CDER has concluded that no significant environmental effects are expected from the issuance of Final Administrative Order OTC000039, and an EIS will not be prepared. A Finding of No Significant Impact is recommended.

5. References

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