

Coast Guard will refer to NVIC 01–2011 for process information and guidance in evaluating SPLNG’s WSA. NVIC 01–2011 is available in the docket where indicated under **ADDRESSES** and also on the Coast Guard’s website at <https://www.dco.uscg.mil/Portals/9/DCO%20Documents/5p/5ps/NVIC/2011/NVIC%2001-2011%20Final.pdf>.

#### IV. Public Participation and Request for Comments

We encourage you to submit comments through the Federal portal at <http://www.regulations.gov>. If your material cannot be submitted using <http://www.regulations.gov>, contact the person in the **FOR FURTHER INFORMATION CONTACT** section of this document for alternate instructions. In your submission, please include the docket number for this notice of inquiry and provide a reason for each suggestion or recommendation.

We accept anonymous comments. All comments received will be posted without change to <http://www.regulations.gov> and will include any personal information you have provided. For more about privacy and the docket, visit <http://www.regulations.gov/privacyNotice>.

Documents mentioned in this notice of inquiry as being available in the docket, and all public comments, will be in our online docket at <http://www.regulations.gov> and can be viewed by following that website’s instructions.

This document is issued under authority of 5 U.S.C. 552 (a).

Dated: July 2, 2018.

**Jacqueline Twomey,**

*Captain, U.S. Coast Guard, Captain of the Port Marine Safety Unit Port Arthur.*

[FR Doc. 2018–14596 Filed 7–6–18; 8:45 am]

**BILLING CODE 9110–04–P**

## DEPARTMENT OF HOMELAND SECURITY

### U.S. Customs and Border Protection

#### Notice of Issuance of Final Determination Concerning Malarone Tablets

**AGENCY:** U.S. Customs and Border Protection, Department of Homeland Security.

**ACTION:** Notice of final determination.

**SUMMARY:** This document provides notice that U.S. Customs and Border Protection (“CBP”) has issued a final determination concerning the country of origin of Malarone tablets. Based upon the facts presented, CBP has concluded that the country of origin of the

Malarone tablets is Canada for purposes of U.S. Government procurement.

**DATES:** This final determination was issued on July 2, 2018. A copy of the final determination is attached. Any party-at-interest may seek judicial review of this final determination within August 8, 2018.

**FOR FURTHER INFORMATION CONTACT:** Ross M. Cunningham, Valuation and Special Programs Branch, Regulations and Rulings, Office of Trade, (202) 325–0034.

**SUPPLEMENTARY INFORMATION:** Notice is hereby given that on July 2, 2018, pursuant to subpart B of Part 177, U.S. Customs and Border Protection Regulations (19 CFR part 177, subpart B), CBP issued one final determination concerning the country of origin of Malarone tablets, which may be offered to the U.S. Government under an undesignated government procurement contract. This final determination (HQ H290684) was issued under procedures set forth at 19 CFR part 177, subpart B, which implements Title III of the Trade Agreements Act of 1979, as amended (19 U.S.C. 2511–18). In the final determination, CBP concluded that the processing in Canada will result in a substantial transformation. Therefore, the country of origin for purposes of U.S. Government procurement of the Malarone tablets is Canada.

Section 177.29, CBP Regulations (19 CFR 177.29), provides that a notice of final determination shall be published in the **Federal Register** within 60 days of the date the final determination is issued. Section 177.30, CBP Regulations (19 CFR 177.30), provides that any party-at-interest, as defined in 19 CFR 177.22(d), may seek judicial review of a final determination within 30 days of publication of such determination in the **Federal Register**.

Dated: July 2, 2018.

**Alice A. Kipel,**

*Executive Director, Regulations and Rulings, Office of Trade.*

HQ H290684

July 2, 2018

OT:RR:CTF:VS H290684 RMC

CATEGORY: Origin

Nicolas Guzman  
Drinker Biddle & Reath LLP  
1500 K Street NW  
Suite 1100

Washington, DC 20005–1209

Re: U.S. Government Procurement;

Country of Origin of Malarone  
Tablets; Substantial Transformation

Dear Mr. Guzman:

This is in response to your letter, dated September 13, 2017, requesting a

final determination on behalf of GlaxoSmithKline LLP (“GSK”) pursuant to subpart B of Part 177 of the U.S. Customs and Border Protection (“CBP”) Regulations (19 C.F.R. Part 177). A teleconference was held with counsel for GSK on June 8, 2018.

This final determination concerns the country of origin of Malarone tablets. As a U.S. importer, GSK is a party-at-interest within the meaning of 19 C.F.R. § 177.22(d)(1) and is entitled to request this final determination.

#### FACTS:

GSK is a global healthcare company that researches, develops, and manufactures pharmaceutical medicines, vaccines, and consumer healthcare products. At issue in this case are tablets sold under the brand name Malarone, which are indicated for the prevention and treatment of acute, uncomplicated *Plasmodium falciparum* malaria. GSK states that Malarone tablets have been shown to be effective in regions where other malaria drugs such as chloroquine, halofantrine, mefloquine, and amodiaquine may have unacceptable failure rates, presumably due to drug resistance.

According to the FDA prescribing information, Malarone is a fixed-dose combination of atovaquone and proguanil hydrochloride. See Prescribing Information, [https://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4089b1\\_05\\_05\\_atovaquone.pdf](https://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4089b1_05_05_atovaquone.pdf) (last visited Dec. 11, 2017). The chemical name of atovaquone 11 is trans-2-[4-(4-chlorophenyl)cyclohexyl]-3-hydroxy-1,4-naphthalenedione and the molecular formula for atovaquone is C<sub>22</sub>H<sub>19</sub>ClO<sub>3</sub>. The chemical name of proguanil hydrochloride is 1-(4-chlorophenyl)-5-isopropyl-biguanide hydrochloride and the chemical formula for proguanil hydrochloride is C<sub>11</sub>H<sub>16</sub>ClN<sub>5</sub>•HCl. Each Malarone Tablet contains 250 milligrams of atovaquone and 100 milligrams of proguanil hydrochloride.

The FDA prescribing information also describes the microbiology or “mechanism of action” of atovaquone and proguanil hydrochloride. It states that atovaquone and proguanil hydrochloride “interfere with 2 different pathways involved in the biosynthesis of pyrimidines required for nucleic acid replication. Atovaquone is a selective inhibitor of parasite mitochondrial electron transport. Proguanil hydrochloride primarily exerts its effect by means of the metabolite cycloguanil, a dihydrofolate reductase inhibitor. Inhibition of dihydrofolate reductase in the malaria

parasite disrupts deoxythymidylate synthesis.”

GSK notes that atovaquone by itself is not indicated for the prevention or treatment of malaria. By itself, atovaquone is used for other purposes, such as the treatment of acute pneumocystis carinii pneumonia and cerebral toxoplasmosis. In contrast, proguanil hydrochloride can be used to treat malaria. However, GSK cites to several academic studies that conclude that the combination of atovaquone and proguanil hydrochloride provides a more effective treatment compared to taking proguanil hydrochloride alone. GSK therefore states that atovaquone and proguanil are “synergistic in their mechanisms of action,” resulting in the increased effectiveness of Malarone tablets compared to taking atovaquone or proguanil hydrochloride alone.

The manufacturing process for GSK’s Malarone tablets begins in India, where the Malarone tablets’ two active pharmaceutical ingredients (“APIs”), atovaquone and proguanil hydrochloride, are manufactured. After the two APIs are manufactured in India, they are imported into Canada for further processing at GSK’s Mississauga, Ontario facility (“GSK Canada”). At GSK Canada, the two APIs are combined in a process that begins by producing a dry mix of the APIs, low-substituted hydroxypropyl cellulose NF, microcrystalline cellulose NF, and sodium starch glycolate NF. The dry mix is then combined with the following inactive ingredients, which are each sourced from the United States or a TAA-eligible country, to produce granules:

- Povidone K30 USP
- Polaxamer 188 NF
- Sofium Starch Glycolate NF
- Hydroxy Propyl Cellulose NF
- Purified Water USP
- Microcrystalline Cellulose NF
- Alcohol USP

Next, the granules are dried, milled into a dry powder, blended with magnesium stearate NF, and compressed into tablets. Finally, a film coat mix is added and the tablets are polished.

Once the manufacturing process is complete, the finished Malarone tablets are exported to a GSK facility in Zebulon, North Carolina. There, the tablets are packaged and labeled for sale to Prasco Laboratories, which markets and distributes the tablets under their own labeling as an authorized generic product under an agreement with GSK.

#### ISSUE:

What is the country of origin of the Malarone tablets for purposes of U.S. Government procurement?

#### LAW AND ANALYSIS:

CBP issues country of origin advisory rulings and final determinations as to whether an article is or would be a product of a designated country or instrumentality for the purposes of granting waivers of certain “Buy American” restrictions in U.S. law or practice for products offered for sale to the U.S. Government, pursuant to subpart B of Part 177, 19 C.F.R. § 177.21 *et seq.*, which implements Title III of the Trade Agreements Act of 1979, as amended (19 U.S.C. § 2511 *et seq.*).

Under the rule of origin set forth under 19 U.S.C. § 2518(4)(B):

An article is a product of a country or instrumentality only if (i) it is wholly the growth, product, or manufacture of that country or instrumentality, or (ii) in the case of an article which consists in whole or in part of materials from another country or instrumentality, it has been substantially transformed into a new and different article of commerce with a name, character, or use distinct from that of the article or articles from which it was so transformed.

See also 19 C.F.R. § 177.22(a).

A substantial transformation occurs when an article emerges from a process with a new name, character, and use different from that possessed by the article prior to processing. A substantial transformation will not result from a minor manufacturing or combining process that leaves the identity of the article intact. See *United States v. Gibson-Thomsen Co.*, 27 C.C.P.A. 267 (1940); and *National Juice Products Ass’n v. United States*, 628 F. Supp. 978 (Ct. Int’l Trade 1986).

In determining whether a substantial transformation occurs in the manufacture of chemical products such as pharmaceuticals, CBP has consistently examined the complexity of the processing and whether the final article retains the essential identity and character of the raw material. To that end, CBP has generally held that the processing of pharmaceutical products from bulk form into measured doses does not result in a substantial transformation of the product. See, e.g., Headquarters Ruling (“HQ”) 561975, dated April 3, 2002; HQ 561544, dated May 1, 2000; HQ 735146, dated November 15, 1993; HQ H267177, dated November 5, 2016; HQ H233356, dated December 26, 2012; and, HQ 561975, dated April 3, 2002. However, where the processing from bulk form into measured doses involves the combination of two or more APIs, and

the resulting combination offers additional medicinal benefits compared to taking each API alone, CBP has held that a substantial transformation occurred. See, e.g., HQ 563207, dated June 1, 2005.

For example, in HQ 563207, CBP held that the combination of two APIs to form Actoplus Met, an alternative treatment for type 2 diabetes, constituted a substantial transformation. The first API, Pioglitazone HCl sourced from Japan or other countries, functioned as an insulin sensitizer that targets insulin resistance in the body. The second API, biguanide sourced from Japan, Spain, and other countries, functioned to decrease the amount of glucose produced by the liver and make muscle tissue more sensitive to insulin so glucose can be absorbed. In Japan, the two APIs were mixed together to form a fixed-combination drug called Actoplus Met. In holding that a substantial transformation occurred when the APIs were combined in Japan to produce Actoplus Met, CBP emphasized that “[w]hile we note that pioglitazone and metformin may be prescribed separately, the final product, Actoplus Met, increases the individual effectiveness of pioglitazone and metformin in treating type 2 diabetes patients.”

Similarly, in HQ H253443, dated March 13, 2015, CBP held that the combination of two APIs in China to produce Prepopik, “a dual-acting osmotic and stimulant laxative bowel preparation for a colonoscopy in adults,” constituted a substantial transformation. Although the importer claimed that Country A-origin sodium picosulfate was the only API in Prepopik, CBP found that the Country B-origin magnesium oxide ingredient also qualified as an API. CBP further found that taking Prepopik had “a more stimulative laxative effect” than taking each of the APIs individually and therefore held that a substantial transformation occurred when the APIs were combined in China.

Here, as in HQ 563207 and HQ H253443, two separate APIs are mixed to create a fixed combination drug that offers additional medicinal benefits compared to taking each API alone. The first API, atovaquone, is not indicated for the prevention or treatment of malaria. The second API, proguanil hydrochloride, is used to treat malaria, but is less effective than Malarone. This is because of the “synergies in [the APIs’] method of action,” which result in a product that “interfere[s] with 2 different pathways” to prevent and treat malaria. Under these circumstances, the combination of atovaquone, proguanil

hydrochloride, and inactive ingredients to form Malarone tablets in Canada results in a substantial transformation. The country of origin of the Malarone tablets is therefore Canada.

**HOLDING:**

The country of origin of the Malarone tablets for purposes of U.S. Government procurement is Canada.

Notice of this final determination will be given in the **Federal Register**, as required by 19 C.F.R. § 177.29. Any party-at-interest other than the party which requested this final determination may request, pursuant to 19 C.F.R. § 177.31, that CBP reexamine the matter anew and issue a new final determination. Pursuant to 19 C.F.R. § 177.30, any party-at-interest may, within 30 days of publication of the **Federal Register** Notice referenced above, seek judicial review of this final determination before the Court of International Trade.

Sincerely,

Alice A. Kipel,  
Executive Director, Regulations & Rulings  
Office of Trade.

[FR Doc. 2018-14632 Filed 7-6-18; 8:45 am]

**BILLING CODE 9111-14-P**

**DEPARTMENT OF THE INTERIOR**

**Fish and Wildlife Service**

[FWS-R4-ES-2015-N040;  
FXES1113040000C2-156-FF04E00000]

**Endangered and Threatened Wildlife and Plants; Draft Recovery Plan for Coquí Llanero**

**AGENCY:** Fish and Wildlife Service, Interior.

**ACTION:** Notice of availability and request for public comment.

**SUMMARY:** We, the U.S. Fish and Wildlife Service, announce the availability of the draft recovery plan for the endangered coquí llanero, a frog endemic to Puerto Rico. The draft recovery plan includes specific recovery objectives and criteria that must be met in order for us to remove this species from listing under the Endangered Species Act of 1973, as amended. We request review and comment on this draft recovery plan from local, State, and Federal agencies, and the public.

**DATES:** In order to be considered, comments on the draft recovery plan must be received on or before September 7, 2018.

**ADDRESSES:**

*Document availability:* You may obtain a copy of this draft recovery plan

by contacting Jan Zegarra, U.S. Fish and Wildlife Service, Caribbean Ecological Services Field Office, P.O. Box 491, Boquerón, PR 00622; tel. (787) 851-7297; or by visiting the Service's Caribbean Field Office website at <https://www.fws.gov/caribbean/ES/Index.html>.

*Comment submission:* You may submit comments by one of the following methods:

1. Submit written comments and materials by mail or hand-delivery to Jan Zegarra, at the above address.
2. Fax them to (787) 851-7440.
3. Send comments by email to [jan\\_zegarra@fws.gov](mailto:jan_zegarra@fws.gov). Please include "Coquí llanero Draft Recovery Plan Comments" in the subject line.

For additional information about submitting comments, see Request for Public Comments.

**FOR FURTHER INFORMATION CONTACT:** Jan Zegarra at (787) 851-7297, or see **ADDRESSES** for further methods of contact.

**SUPPLEMENTARY INFORMATION:** We, the U.S. Fish and Wildlife Service, announce the availability of the draft recovery plan for the endangered coquí llanero (*Eleutherodactylus juanariveroi*). The draft recovery plan includes specific recovery objectives and criteria that must be met in order for us to remove this species from listing under the Endangered Species Act of 1973, as amended (ESA; 16 U.S.C. 1531 *et seq.*). We request review and comment on this draft recovery plan from local, State, and Federal agencies and the public.

**Background**

The coquí llanero is a small frog species endemic to Puerto Rico. In 2007, it was described as a new species of the genus *Eleutherodactylus*, family Leptodactylidae. Males measure approximately 0.58 in (14.7 mm), and females 0.62 in (15.8 mm). It has the smallest clutch size of all *Eleutherodactylus* species on Puerto Rico, and a high-frequency call. The only population estimate available for the coquí llanero indicates a mean population size of  $473.3 \pm 186$  individuals per ha (or 192 per ac; Ríos-López pers. comm. 2011).

The coquí llanero is currently known to be restricted to one freshwater herbaceous wetland in the municipality of Toa Baja, Puerto Rico. The herbaceous vegetation in the wetland consists of *Blechnum serrulatum* (toothed midorus fern), *Thelypteris interrupta* (willdenow's maiden fern), *Sagittaria lancifolia* (bulltongue arrowhead), *Cyperus* sp. (flatsedges), *Eleocharis* sp. (spike rushes), and vines

and grasses (Ríos-López and Thomas 2007). The species is currently threatened by the combined influences of urban development, activities associated with the operation and future closure of the Toa Baja municipal landfill, activities associated with clearing water channels for flood control, and invasive wetland plant species. Additional threats include restricted distribution and highly specialized ecological requirements, which may exacerbate other potential threats like landfill leachate pollution, the use of herbicides, brush fires, competition, and environmental effects resulting from climate change.

Under the ESA, the Service added the coquí llanero as an endangered species to the Federal List of Endangered and Threatened Wildlife in title 50 of the Code of Federal Regulations on October 4, 2012 (77 FR 60778). The 2012 final rule also designated critical habitat, covering an area of 615 ac (249 ha), for the species.

The recovery strategy for the coquí llanero includes protection and management of occupied habitat and suitable unoccupied habitat for potential future introductions, and addresses immediate threats that led to its listing. Because of stressors like reduced geographic distribution, limited dispersal capabilities, and the species' specialized breeding requirements, the species is likely to have reduced adaptive capacity. Therefore, in order to meet the recovery goal of delisting, we must increase the number of coquí llanero populations. This strategy seeks to safeguard the only existing coquí llanero population in case the species does not withstand or recover from a stochastic or catastrophic event.

Section 4(f) of the ESA requires the development of recovery plans for listed species, unless such a plan would not promote the conservation of a particular species. Recovery plans describe actions considered necessary for conservation of the species, establish criteria for downlisting or delisting, and estimate time and cost for implementing recovery measures. Section 4(f) of the ESA also requires us to provide public notice and an opportunity for public review and comment during recovery plan development. We will consider all information presented during a public comment period prior to approval of each new or revised recovery plan. We and other Federal agencies will take these comments into account in the course of implementing approved recovery plans.