The meropenem docket remained opened for public comment from February 27, 2012, until March 28, 2012. There were no comments submitted to the docket during that time. The key findings of this final clinical study report are:

The submitted study was an open-label, non-comparative, multicenter, prospective, multiple pharmacokinetic (PK) and safety study in infants less than 91 days of age. The study enrolled 200 infants with a median postnatal age of 21 days (range 1 to 92 days) and a median gestation age (GA) of 27.8 weeks (range 22.5 to 40 weeks). Infants with complicated intra-abdominal infections who were receiving meropenem based on local standard of care were eligible for enrollment. Complicated intra-abdominal infections were defined per the protocol as physical, radiologic, or bacteriologic findings of complicated intra-abdominal infection to include peritonitis, necrotizing enterocolitis (NEC) grade II or higher by Bell's criteria, Hirschsprung's disease with perforation, spontaneous perforation, meconium ileus with perforation, bowel obstruction with perforation, as evidenced by free peritoneal air on abdominal radiograph, intestinal pneumatosis, or portal venous gas on abdominal radiographic examination, or possible NEC.

The study was not statistically powered to establish efficacy because the Division of Anti-Infective Products agreed that extrapolation of efficacy to pediatric populations from adult populations was acceptable. However, clinical efficacy endpoints were also evaluated. The efficacy assessment included a comparison of the clinical status at study baseline and at day 28 or after a minimum of 7 days of treatment, using a combination of an assessment using the Score for Neonatal Acute Physiology II tool and other protocol specified outcome criteria. The clinical endpoint was defined as the patient being alive, with negative bacterial cultures from a sterile body fluid, and a presumptive clinical cure. Clinical failure was defined as death, change in antibiotic therapy while on study drug, or lack of presumptive clinical cure. The addition of treatment directed against Gram-positive pathogens from a non-abdominal source was not considered to represent treatment failure. Using these criteria, 195/200 patients or 97.5 percent were considered to have achieved the clinical endpoint. Of the 195 patients included in the efficacy population, 192 (98.5 percent) were evaluated for efficacy. The overall efficacy success rate for the study was 84.4 percent (95 percent confidence interval, 78.5 to 89.2 percent).

Analysis of safety was a primary objective of the study. The following assessments were included in the study: Monitoring for adverse events, serious adverse events, and death; documentation of seizures; acute abdominal complications; development of resistant bacterial infection or candidiasis; treatment failure; physical examination; clinical laboratory values; cultures from sterile sites, and concomitant medications. There were 11 deaths in the study; all occurred in patients less than 32 weeks GA. The most common cause of death was multi-organ failure. None of the deaths were related to meropenem administration. The following adverse events occurred with a frequency in the study that differed from that seen in previous pediatric and adult studies: Convulsion (seizures), 5 percent, hyperbilirubinemia, 4.5 percent and vomiting, 2.5 percent. Study oversight included a safety committee and an independent data safety monitoring board.

The Division of Anti-Infective Products agreed that meropenem was well-tolerated in the pediatric population enrolled in the study. Of the 10 patients with seizures, 8 patients were adjudicated to have developed seizures possibly due to the study medication. Because cerebrospinal fluid was only evaluated in a limited number of patients with seizures, it is not possible to determine if the seizure threshold may have changed due to possible underlying meningitis and the administration of meropenem.

II. Recommendation

This study supports the use of meropenem in neonates and infants less than 91 days of age for complicated intra-abdominal infections. However, infants with complicated intra-abdominal infections are anticipated to have different physiological characteristics than patients with meningitis that may impact the PK of meropenem; as such, it may not be appropriate to apply the PK findings from this population to a patient population with meningitis. The Division recommended that the evaluation of meropenem in infants less than 91 days of age be limited to the treatment of complicated intra-abdominal infections at this time.

FDA's requested labeling changes, including dosing recommendations for the use of meropenem in neonates and infants less than 91 days of age for complicated intra-abdominal infections, are available on the FDA Web site at *http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm379088.htm* and in the docket (Ref. 1).

Dated: May 21, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–12848 Filed 5–27–15; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2015–N–0012]

Molecular Characterization of Multiple Myeloma Black/African Ancestry Disparity

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of grant funds for the support of the efforts of the Center for Drug Evaluation and Research (CDER). FDA is announcing its intent to accept and consider a single-source application for the award of a grant to the Multiple Myeloma Service of Memorial Sloan Kettering Cancer Institute. The goal of the cooperative agreement between CDER and the Multiple Myeloma Service of Memorial Sloan Kettering Cancer Institute is to support the development of appropriate methodologies to conduct clinical trial design evaluation and determine extrapolation of findings from the general population to the U.S. Black population.

DATES: Important dates are as follows:

1. The application due date is July 20, 2015.
2. The anticipated start date is August 2015.
3. The opening date is May 18, 2015.
4. The expiration date is July 21, 2015.

ADDRESSES: Submit electronic applications to: *http://www.Grants.gov.* For more information, see section III of the **SUPPLEMENTARY INFORMATION** section of this notice.

FOR FURTHER INFORMATION CONTACT: Dickran Kazandjian, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2320, Silver Spring, MD 20993–0002, 240–402–5272; or Vieda Hubbard, Division of Acquisition Support and Grants (HFA–500), Food and Drug

Administration, 5630 Fishers Lane, Rockville, MD 20857, 240–402–7588.

For more information on this funding opportunity announcement (FOA) and to obtain detailed requirements, please refer to the full FOA located at: *http://www.grants.gov.* Search by Funding Opportunity Number: RFA–FD–15–029.

SUPPLEMENTARY INFORMATION:

I. Funding Opportunity Description

RFA–FD–15–029
93.103

A. Background

Multiple Myeloma (MM) is mainly a disease of older adults with a median diagnosis age of 65 years and patients younger than 40 represent only 2 percent of diagnoses. In the United States, 20,000 new cases are diagnosed annually. Although the etiology of MM remains elusive, clinical features, observed racial disparity patterns of incidence, reported familial clustering, and younger incidence in patients of Black/African ancestry suggests a role for susceptibility genes. Novel therapies have revolutionized treatment of MM and much of current research is focused on identifying not only efficacious drugs but also on the most efficacious time to initiate treatment. MM is a spectrum of disease which is first manifested by its precursor state Monoclonal gammopathy of undetermined significance (MGUS) which then evolves into smoldering myeloma and then finally symptomatic myeloma and therefore some paradigms of treatment initiation are evolving. Much of this work involves identifying the molecular aberrations, which classify patients' risks. However, this work has mostly been done on the population as a whole. Despite that MM in patients of Black ancestry clearly has a biologically different natural history; clinically Blacks are assessed using the same genetic approaches as the whole population. The proposed project will afford us the opportunity to identify and characterize MM in the Black population with much higher genetic and molecular resolution. It will answer questions such as whether Blacks have, in general, better survival because of the presence of more low risk genetic aberrations and whether these changes alter the effect of treatment drug. Our conclusions may have immense regulatory impact. For example, certain MM therapies may be indicated sooner in the treatment course in Blacks. Alternatively, some therapies may be found to have minimal efficacy and indication in Blacks with certain molecular subtypes. This proposal will be the first study to characterize the molecular subtypes of MM in Blacks in a systematic fashion, investigate the effect of these on novel therapy outcomes, and potentially have major impact on regulatory approvals of future therapies. Therefore, it is imperative to focus on this under-represented population and at least begin to understand the differences in MM pathophysiology, which may ultimately lead to improved outcomes.

The Memorial Sloan Kettering Cancer Institute has established a cohort of Black/African ancestry patients diagnosed with MM. These patients have been previously enrolled onto clinical trials and bone marrow biopsy tissue samples are available along with peripheral blood samples all banked. Furthermore, there has been close monitoring of these patients and detailed clinical data already exist. This is crucial to the project. Memorial Sloan Kettering is uniquely positioned to provide FDA much required data both by their novel technical platform and also by their available unique patient cohort and biopsy samples. Finally, organized involvement among a number of Sloan Kettering/National Cancer Institute (NCI)/FDA working groups on issues related to endpoints in MM which provides the unique ability to collaboratively engage FDA, patients, academics, government and industry so that any important findings may distributed to the community will be required.

B. Research Objectives

The research objective is to characterize the molecular subtypes of MM in patients of Black/African ancestry and investigate the effect of these *on prognosis* and novel therapy outcomes.

C. Eligibility Information

The following organization is eligible to apply: The Multiple Myeloma Service of the Memorial Sloan Kettering Cancer Institute. This is a sole source request for application because the Multiple Myeloma Service of the Memorial Sloan Kettering Cancer Institute is uniquely situated to support FDA's scientific mission of protecting and promoting the public health by initiating and facilitating research into demographic subpopulations of the United States. It has both the required patient population and the proprietary technical assays required to perform the proposed work.

II. Award Information/Funds Available

A. Award Amount

It is anticipated that FDA/CDER will fund this Cooperative Agreement up to $172,000 in Fiscal Year (FY) 2015 and $106,000 in FY 2016 in support of this program project. It is anticipated that only one award will be made, not to exceed $278,000 (direct plus indirect) for total costs. Awards are contingent upon the availability of funds.

B. Length of Support

Two-year period of performance beginning on August 2015 or date of award.

III. Electronic Application, Registration, and Submission

Only one electronic application will be accepted. To submit an electronic application in response to this FOA, the applicant should first review the full announcement located at *http://www.Grants.gov.* Search by Funding Opportunity Number: RFA–FD–15–029. (FDA has verified the Web site addresses throughout this document, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.) For the electronically submitted application, the following steps are required.

- Step 1: Obtain a Dun and Bradstreet (DUNS) Number
- Step 2: Register With System for Award Management (SAM)
- Step 3: Obtain Username & Password on *http://www.Grants.gov*
- Step 4: Authorized Organization Representative (AOR) Authorization
- Step 5: Track AOR Status
- Step 6: Register With Electronic Research Administration (eRA) Commons

Steps 1 through 5, in detail, can be found at *http://www07.grants.gov/applicants/organization_registration.jsp.* Step 6, in detail, can be found at *https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp.* After you have followed these steps, submit the electronic application to: *http://www.grants.gov.*

Dated: May 20, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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