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RESEARCH**

*APPLICATION NUMBER:*

**21-092**

**APPROVAL LETTER**

NDA 21-092

Metabolic Solutions, Inc.  
Attention: David A. Wagner, Ph.D.  
President  
460 Amherst Street  
Nashua, NH 03063

Dear Dr. Wagner:

Please refer to your new drug application (NDA) dated March 17, 1999, received March 19, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Helicosol (<sup>13</sup>C-urea) 125mg lyophilized powder.

We acknowledge receipt of your submissions dated May 5, 1999, June 7, 1999, July 30, 1999, August 26, 1999, November 16, 1999, and December 15, 1999.

This new drug application provides for the use of Helicosol (<sup>13</sup>C-urea) lyophilized powder in conjunction with the Ez-HBT™ test for the detection of <sup>13</sup>CO<sub>2</sub> in whole blood specimens, collected after the ingestion of <sup>13</sup>C-urea.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text, submitted to the Agency on December 16, 1999. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted labeling (text for the package insert, immediate container and carton labels submitted December 15, 1999). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-092." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We note that you have not fulfilled the requirements of 21 CFR

314.55 (or 601.27). We are deferring submission of your pediatric studies until March 31, 2003. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at [www.fda.gov/cder/pediatric](http://www.fda.gov/cder/pediatric)) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit and notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

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We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Jeffrey Fritsch, R.Ph., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

Mark J. Goldberger, M.D., M.P.H.

Director

Division of Special Pathogen and Immunologic Drug Products

Office of Drug Evaluation IV

Center for Drug Evaluation and Research