NHIA
National Home Infusion Association
Providing solutions for the infusion therapy community

March 4, 2014

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: "List of Bulk Drug Substances That May Be Used in Pharmacy Compounding; Bulk Drug Substances That May Be Used to Compound Drug Products in Accordance With Section 503A of the Federal Food, Drug, and Cosmetic Act"

Docket Number: FDA–2013-N-1525

Dear Commissioner Hamburg:

The National Home Infusion Association (NHIA) submits these comments on the draft guidance made available on December 4, 2013 by the Food and Drug Administration (FDA) entitled "List of Bulk Drug Substances That May Be Used in Pharmacy Compounding; Bulk Drug Substances That May Be Used to Compound Drug Products in Accordance With Section 503A of the Federal Food, Drug, and Cosmetic Act." NHIA is a national membership association for clinicians, managers and organizations providing infusion therapy services for patients in the home and outpatient settings.

NHIA understands that FDA is obligated by Section 503A to develop a Bulk Drug Substances List and in carrying out these obligations the NHIA recommends that the FDA utilize a transparent and open process that provides stakeholders with meaningful opportunity to comment on the products that the FDA proposes to include on these lists. Specifically, NHIA recommends that the FDA utilize a formal notice and comment period not only for establishing this list, but also for updating it.

In addition, we believe that the FDA should conduct public meetings related to the list for interested stakeholders to discuss which bulk drug substances should initially be included on the lists. FDA also should meet with provider groups and trade associations to discuss the bulk drug substances being considered for the lists. We believe that soliciting feedback through several channels is important to ensure that the FDA obtains the most helpful and current advice about the appropriate bulk drug substances to be included on the list. After the FDA receives feedback through these channels, NHIA

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recommends that the FDA issue the list in proposed form so that stakeholders have the opportunity to comment on the bulk drug substances included therein.

In addition, the FDA should regularly update the list by an open process that provides stakeholders with meaningful opportunities to provide comments. The FDA may consider establishing a regular schedule under which the Agency requests nominations for bulk substances that should be added to or removed from the list, considers the feedback received, and updates the list accordingly. This predictable and transparent process will encourage stakeholders to continuously invest time in preparing and submitting thoughtful, evidence-based recommendations of the bulk substances that the FDA should consider adding to or removing from the list.

Also, due to the unique needs of each individual patient and the lag between scientific developments and regulatory updates, NHIA believes that the FDA should establish a process for physicians and pharmacists to petition to have a bulk substance made available for compounding even if it is not on the approved bulk substances list. Should a drug shortage occur where a bulk substance is needed for a drug it may become imperative that a process be in place to move swiftly to make the bulk substance available for compounding.

NHIA's nominations and responses to the FDA's use information questions for the initial bulk substances list are as follows:

L-Glutamic Acid

Bulk Drug Substance

- Ingredient name:
  L-Glutamic Acid
- Chemical name:
  (S)-2-Aminopentanedioic acid, Glu
- Common name(s):
  L-Taurine
- Chemical grade or description of the strength, quality, and purity of the ingredient:
  PharmaGrade
- Information about how the ingredient is supplied (e.g., powder, liquid):
  Powder
  Manufactured by Ajinomoto
  Manufactured under appropriate GMP controls for pharma or biopharmaceutical production
  Suitable for cell culture
- Information about recognition of the substance in foreign pharmacopeias and the status of its registration(s) in other countries, including whether

information has been submitted to USP for consideration of monograph development:

Already exists in European Pharmacopeia (EP).

- A bibliography of available safety and efficacy data, [3] including any relevant peer-reviewed medical literature:

  Amino acid in standard commercially available amino acid preparations.

Compounded Product

- Information about the dosage form(s) into which the drug substance will be compounded (including formulations):

  Product is weighed out, then diluted in sterile water along with other amino acids, pH is buffered and final product is filtered through a 0.2 Micron filter for IV administration.
- Information about the strength(s) of the compounded product(s):

  Final product prepared is a 10% amino acid preparation with fifteen other amino acids/products.
- Information about the anticipated route(s) of administration of the compounded product(s):

  Route of administration is IV once further combined with other nutrients to prepare a TNA.
- Information about the past and proposed use(s) of the compounded product(s), including the rationale for its use or why the compounded product(s), as opposed to an FDA-approved product, is necessary:

  Amino acid preparation used to treat patients with MSUD that cannot metabolize the branch chain amino acids found in commercially available amino acid products.
- Available stability data for the compounded product(s):

  Product sent to outside lab for validation of 35 days refrigerated and re-validated every quarter.

L-Taurine

Bulk Drug Substance

- Ingredient name:

  L-Taurine
- Chemical name:

  2-Aminoethanesulfonic acid
- Common name(s):

  L-Taurine
- Chemical grade or description of the strength, quality, and purity of the ingredient:

PharmaGrade

- Information about how the ingredient is supplied (e.g., powder, liquid):
  Powder
  Manufactured by Ajinomoto
  Manufactured under appropriate GMP controls for pharma or biopharmaceutical production
  Suitable for cell culture
- Information about recognition of the substance in foreign pharmacopeias and the status of its registration(s) in other countries, including whether information has been submitted to USP for consideration of monograph development:
  Taurine is in the USP monographs, L-Taurine is not.
- A bibliography of available safety and efficacy data, [3] including any relevant peer-reviewed medical literature:
  Amino acid in standard commercially available amino acid preparations.

Compounded Product

- Information about the dosage form(s) into which the drug substance will be compounded (including formulations):
  Product is weighed out, then diluted in sterile water along with other amino acids, pH is buffered and final product is filtered through a 0.2 Micron filter for IV administration.
- Information about the strength(s) of the compounded product(s):
  Final product prepared is a 10% amino acid preparation with fifteen other amino acids/products.
- Information about the anticipated route(s) of administration of the compounded product(s):
  Route of administration is IV once further combined with other nutrients to prepare a TNA.
- Information about the past and proposed use(s) of the compounded product(s), including the rationale for its use or why the compounded product(s), as opposed to an FDA-approved product, is necessary:
  Amino acid preparation used to treat patients with MSUD that cannot metabolize the branch chain amino acids found in commercially available amino acid products.
- Available stability data for the compounded product(s):
  Product sent to outside lab for validation of 35 days refrigerated and re-validated every quarter.

Please feel free to have your staff contact Kendall Van Pool, NHIA Vice President of Legislative Affairs, at (703) 838-2664 or kendallvanpool@nhia.org should you want to discuss our comments further. Thank you for your consideration of NHIA's comments.

Sincerely,

Russell Bodoff
President & CEO
National Home Infusion Association