CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205109Orig1s000

CHEMISTRY REVIEW(S)
NDA 205-109

Velphoro™ (Suroferric oxyhydroxide) 500 mg
Chewable Tablet)

Vifor Fresenius Medical Care Renal Pharma

Thomas M. Wong, Ph.D.
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment

Division of Cardiovascular and Renal Products
Review of Chemistry, Manufacturing, and Controls
Table of Contents

The Executive Summary ........................................................................................................................................7

I. Recommendations ........................................................................................................................................7
   A. Recommendation and Conclusion on Approvability ............................................................................7
   B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk
      Management Steps, if Approvable ........................................................................................................7

II. Summary of Chemistry Assessments .......................................................................................................7
   A. Description of the Drug Product(s) and Drug Substance(s) ..............................................................7
   B. Description of How the Drug Product is Intended to be Used ..........................................................8
   C. Basis for Approvability or Not-Approval Recommendation ...............................................................8

III. Administrative ..........................................................................................................................................8
    A. Reviewer’s Signature: See DARRTS .................................................................................................8
    B. Endorsement Block: See DARRTS ....................................................................................................8
    C. CC Block: See DARRTS ....................................................................................................................8

Chemistry Assessment .....................................................................................................................................9

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data .................9
   S. DRUG SUBSTANCE ..............................................................................................................................9
   P. DRUG PRODUCT .................................................................................................................................54
   A. APPENDICES ....................................................................................................................................109
   R. REGIONAL INFORMATION ................................................................................................................109

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1 ............................................110
    A. Labeling & Package Insert ................................................................................................................110
    B. Environmental Assessment Or Claim Of Categorical Exclusion ..................................................115

III. List Of Deficiencies To Be Communicated: .........................................................................................115
1. NDA: 205-109

2. REVIEW #: 1

3. REVIEW DATE: September 27, 2013

4. REVIEWER: Thomas M Wong, Ph.D.

5. PREVIOUS DOCUMENTS:

   Previous Documents                      Document Date
   IND 75,610

6. SUBMISSION(S) BEING REVIEWED:

   Submission(s) Reviewed                  Document Date
   Original submission                      Feb 1, 2013
   Amendment # 0003                         Feb 19, 2013
   Amendment # 0008                         Mar 29, 2013
   Amendment # 0011                         Apr 19, 2013
   Amendment # 0012                         Apr 29, 2013
   Amendment # 0020                         Aug 9, 2013
   Amendment # 0023                         Aug 22, 2013
   Amendment # 0025                         Aug 29, 2013
   Amendment # 0027                         Sep 19, 2013
   Amendment # 0028                         Sep 24, 2013

7. NAME & ADDRESS OF APPLICANT:

   Name: Vifor Fresenius Medical Care Renal Pharma France
   Address: 12, Rue de la Chaussee d’Antin
            Paris, France, 75009
   Fresenius Medical Care North America
   U.S. Representative: Michael Bauer, Ph.D., Director, Global Regulatory Affairs
   Ruth Turner, Director, Regulatory Affairs Pharmaceuticals
   Telephone: 781-699-4654

8. DRUG PRODUCT NAME/CODE/TYPE:
a) Proprietary Name: Velphoro
b) Non-Proprietary Name (USAN): Sucroferric oxyhydroxide
c) Code Name/# (ONDC only): PA21
d) Chem. Type/Submission Priority (ONDC only):
   • Chem. Type: 5
   • Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(2)

10. PHARMACOL. CATEGORY: Control of serum phosphate levels in patients with end stage renal disease (ESRD)

11. DOSAGE FORM: Chewable tablet

12. STRENGTH/POTENCY: 500 mg iron (III)

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
   _____SPOTS product – Form Completed
   ___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
   USAN: Sucroferric oxyhydroxide
CHEMISTRY REVIEW

Chemistry Review Data Sheet

CAS Name: Mixture of iron(III)-oxyhydroxide, sucrose, Starches
Polynuclear iron(III)-oxyhydroxide stabilized with sucrose, and starches

CAS registry number:

- β-iron(III)-oxyhydroxide: CAS No. 12134-57-5
- Sucrose: CAS No. 57-50-1
- Starch: CAS No. 9005-25-8

Molecular formula: \( \text{pn-FeOOH} + x \text{C12H22O11} + y \text{(C6H10O5)n} \)

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

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\(^1\) Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:

- 2 – Type 1 DMF
- 3 – Reviewed previously and no revision since last review
- 4 – Sufficient information in application
- 5 – Authority to reference not granted
- 6 – DMF not available
- 7 – Other (explain under "Comments")

Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

### B. Other Documents:

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18. STATUS:

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<td>Thomas Wong</td>
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The Chemistry Review for NDA 205-109

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 205-109 for Velphoro™ (sucroferric oxyhydroxide) chewable tablet, 500 mg, cannot be approved from the CMC perspective due to the following pending issue.

Acceptance of dissolution specification has not been resolved between the biopharmaceutics reviewer and the applicant.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None as per this review.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug product

The applicant has developed a chewable tablet for oral administration for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis. The trade name for sucroferric oxyhydroxide chewable tablet is Velphoro™ and the tablets are red-brown, round, flat-faced chewable tablet embossed with “PA 500” and is approximately Each tablet contains 500 mg elemental iron equivalent to 2500 mg sucroferric oxyhydroxide complex and the following excipients: woodberry flavor, neohesperidin dihydrochalcone, magnesium stearate, and silica. The tablets will be manufactured by Vifor SA in Switzerland and by in Germany. Commercial batch size for the Vifor and facility is tablets and tablets, respectively. Tablets are packaged in HDPE bottles with 30 counts and 90 counts per bottle. Tablets are stored at 25°C (77°F). Excursions are permitted between 15°C and 30°C (59°F and 86°F). Available 18 months stability data supports 30-month expiration dating period for the tablets when packaged in the proposed commercial packages and stored in the afore-mentioned storage conditions.

Drug substance

Sucroferric oxyhydroxide is a complex which consists of the polynuclear iron (III)-oxyhydroxide, sucrose and starch. The pu-FeOOH moiety is produced as an aqueous suspension, it is chemically not stable and cannot be isolated and stored as an active pharmaceutical ingredient. Polynuclear iron (III)-oxyhydroxide is a phosphate binder and exhibits minimal release of iron across the range of pH values found in the GI tract. It adsorbs the dietary phosphate in the GI tract, preventing its
uptake into the blood, and thereby reducing the serum level of phosphorus. The phosphate bound to polynuclear iron (III)-oxyhydroxide is subsequently eliminated in the feces. The polynuclear iron (III)-oxyhydroxide is prepared by

The drug is manufactured in Vifor (International) Inc., in Switzerland. A commercial batch size for PA21 ranging between

B. Description of How the Drug Product is Intended to be Used

The recommended starting dose of Velphoro is 3 tablets (1,500 mg iron) per day, administered as 1 tablet (500 mg iron) 3 times daily with meals. Tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, tablets may be crushed.

C. Basis for Approvability or Not-Approval Recommendation

Adequate information has been provided to allow a satisfactory evaluation of the quality of both drug substance (DS) and drug product (DP). DS and DP manufactured and packaged in accordance with the procedures and proposed specifications to assure their quality throughout shelf life. NDA 205-109 for Velphoro™ (sucroferric oxyhydroxide) 500 mg Chewable Tablet cannot be approved as per CMC perspective due to pending issue mentioned in Section 1A above.

III. Administrative

A. Reviewer’s Signature: See DARRTS

B. Endorsement Block: See DARRTS

C. CC Block See DARRTS

109 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

THOMAS M WONG
09/27/2013

RAMESH K SOOD
09/27/2013
Initial Quality Assessment
Branch I

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Figure 1  Schematic Diagram of the Structure of PA21
Summary
This is an e-CTD 505(b)(1) NDA for a new phosphate binder with the code name PA21 which consists of polynuclear iron (III) oxyhydroxide stabilized with sucrose and mixed with starches. This is formulated into chewable tablets each containing 500 mg iron. The drug is indicated for the control of serum phosphorus levels in patients with end-stage renal disease. Upon oral administration with a meal, phosphate binding takes place in the GI tract by ligand exchange between the hydroxyl groups and/or water and the phosphate ions. Iron is minimally absorbed since the polynuclear iron oxyhydroxide is insoluble. PA21 was developed under IND 75,610 and is intended to be a safe and effective calcium, aluminum and lanthanum free phosphate binder, with a reduced pill burden compared to other approved products for this indication.

There was only one meeting with the firm where CMC topics were discussed, a pre-NDA CMC meeting held on Dec. 7, 2012. The issues covered included the definition of the drug substance, the need for [REDACTED] as part of the drug substance specification.

Agreement was reached that [REDACTED]. Vifor was also told that the Agency did not agree to [REDACTED].

Drug Substance
The Applicant refers to the mixture of polynuclear iron (III) oxyhydroxide (pn-FeOOH) sucrose and starches as the drug substance (PA21). The manufacturing process for PA21 consists of [REDACTED].
It is stated that the quality of the drug substance is not influenced by the scale of manufacture and a commercial batch size of [REDACTED] is proposed.

Specifications are proposed for the drug substance which include the usual test attributes, appearance, identification, LOD, and assay (iron, sucrose and starch) and microbiological quality. In addition, there are tests for particle size, sodium content and in-vitro phosphate adsorption. Batch analysis results for non-clinical, clinical, stability and process validation batches, ranging in size from [REDACTED] have been provided. Both packaging configurations have been used in the stability studies of PA21. Three batches, all over [REDACTED] manufactured in June 2010, and stored at 30°C/75%RH, 25°C/60%RH and 40°C/75% RH have been studied and 12 - 18 months long term data are available. 48 months’ data from two earlier, smaller scale [REDACTED] batches packaged in [REDACTED] are also reported. The stability protocol includes tests for assay (iron, starch, sucrose), iron release, in vitro phosphate adsorption, LOD and particle size. Forced degradation studies have also been conducted. A retest period of [REDACTED] is proposed for the drug substance stored at or below 30°C and packaged in [REDACTED].

**Drug Product**

PA21 chewable tablets are manufactured in only one strength which is equivalent to 500 mg of iron. The tablets are red brown, round, flat faced and approximately 20 mm in diameter and 6 mm in thickness, with a nominal mass of [REDACTED]. The excipients used are magnesium stearate and colloidal silicon dioxide which are compendial as well as Woodberry flavor and the [REDACTED] neohesperidine dihydrochalcone. Woodberry flavor is not in USP or Ph. Eur. but is stated to comply with the European Council Regulation No. 1334/2008 on flavorings. Reference to [REDACTED] is provided. Neohesperidine dihydrochalcone is also not in USP but has a Ph. Eur monograph.

There are two primary drug product manufacturing sites, one at Vifor in Switzerland and the other at [REDACTED] in Germany. The same manufacturing process is used at both sites but the nominal batch sizes are [REDACTED].

The manufacturing process consists of [REDACTED]. The formulation and manufacturing process has evolved from material used for Phase 1 and 2 trials to the current Phase 3 and proposed commercial process.

The manufacturing process development contains some elements of QbD starting with the identification of the QTPP, the related CQAs and risk assessment of the ability of the process to reliably produce product of the intended quality. The functional relationships that link material attributes and process parameters to the CQAs were determined by DoE studies with 2 production scale batches and 20 sub-batches. The tabletting speed, main compression force and
drug substance lot were identified as critical input parameters. A design space was defined for the tabletting speed – a range which was claimed to be confirmed by DOE. The main compression force is the key parameter for setting up the tabletting equipment and must be adjusted based on the physical binding properties of the drug substance lot used for the drug product manufacture. The compression force correlates with tablets hardness and will be set.

PA21 tablets are packaged in HDPE bottles.

The specification proposed for the product includes standard test attributes like ID, assay, LOD, uniformity of dosage units and microbiological quality. In addition, attributes like tablet hardness and disintegration time which are critical for a chewable tablet have been proposed as well as unique critical tests for this drug such as in vitro phosphate adsorption and iron release. There is no impurity specification since it is claimed that there is no impurity in the product which is not present in the drug substance. Batch analysis data have been provided for numerous batches used in the clinical trials as well as commercial scale validation batches manufactured at both Swiss and German sites.

Stability data have been submitted from both manufacturing sites. The batch sizes for the 3 batches each from Vifor, Switzerland and tablets and tablets respectively. Six months’ long term data from the Swiss site and 9 months’ long term data from the German site are available for product packaged in bottles 6 months’ data under accelerated storage conditions have been submitted for both sites. Based on the results from these studies an initial shelf-life of is proposed. In-use stability studies have been carried out on 90 count bottles It is claimed that the test results at the end of support a Other special stability studies performed include bulk tablet storage stability and photostability.

Critical Review Issues

Drugs Substance

- Is the active moiety ferric ion or polynuclear ferric oxyhydroxide?
- The firm had been told earlier that polynuclear ferric oxyhydroxide is not an NME, however recently they have sent in a rebuttal. Does this change our original decision?
- Has the proposed structure of pn-FeOOH been adequately characterized?
- Is the structure of akaganeite (β-FeOOH) well established in the literature? How is it prepared? This is important since it is stated that the XANES spectrum of PA21 batches shows good correlation with the reference spectrum of akaganeite.
- Is the manufacturing process of PA21 described in adequate detail?
- Are the specifications for metallic impurities in the raw material, acceptable? Has a rationale been provided for the selection of metal impurities to be included? Are the proposed acceptance criteria satisfactory? This should be discussed with the pharm/tox reviewer -- they had concerns about levels during development.
- Are the proposals for skip testing of the components, acceptable?
The firm was advised in the pre-NDA meeting to clarify how they monitor reaction completion in the [+] step.

Regarding the specification:
- The Applicant has not yet included the [+] test and states that they are working on it. This should be in place with test results for some batches for completion of the CMC review.
- For many tests, the Applicant has proposed 2 analytical methods e.g. complexometric titration or NIRS for assay of iron, spectrophotometry or ICP-OES for in-vitro phosphate adsorption. For some of these tests they designate one method as the reference method which is presumably the regulatory method. However, they have a footnote to the specification table stating that the reference method is performed at least once a year. Is it clear that the alternate method is performed on every batch at release? Have they demonstrated the equivalency of both methods?
- It is not clear what the applicant means in footnote [+] for microbiological tests.
- Are the acceptance criteria for particle size and in-vitro phosphate adsorption adequately justified?
- The table should be reformatted removing many of the footnotes. References for tests such as microbiological quality should be to USP <61> and <62>.
- It is stated that the iron release test, which was historically included in the stability protocol, will not be part of future stability studies since it is not stability indicating. Is this acceptable? Should this test be done for batch release?
- Is the proposed retest date of [+] for the drug substance acceptable?

**Drug Product**
- Biopharm has indicated that a dissolution test is needed for this product. A method development report has been submitted. Acceptance of the method and limits is the responsibility of the Biopharm reviewer.
- Excipient compatibility with the drug substance should be evaluated.
- How much information has been provided for the [+] neohesperidin dihydrochalcone, since this ingredient doesn’t seem to have been used in US approved drugs?
- The manufacturing process development report should be reviewed in-depth including the DoEs performed.
- Are the in-process parameters and acceptance criteria for [+] the manufacturing process satisfactory?
- Tabletting speed, main compression force and drug substance lot have been identified as critical input parameters and based on DoE and validation studies it is stated that a design
space has been created for these parameters. Is this a bona fide design space or are these merely the validated ranges for the tabletting equipment?

- Has the design space been incorporated into the manufacturing process description (MBR)?

- Regarding the specification:
  - Many of the issues identified with the drug substance specification are also present here – too many footnotes, references to Ph. Eur. when relevant USP methods exist for common attributes such as uniformity of dosage units, microbiological quality etc.
  - Two methods are specified for some tests like ID and in-vitro phosphate adsorption without delineating one as the regulatory and the other as the alternative procedure.
  - The two methods for identification, a color reaction/precipitation of iron versus NIR cannot be considered equivalent since the former only establishes the presence of iron whereas the latter should be specific for the mixture of polynuclear ferric oxyhydroxide, sucrose and starches. The Applicant should be recommended to use both methods for identification.
  - Testing is proposed for microbiological quality.
  - The hardness limits are quite broad considering that this is a critical attribute for chewable tablets. Are different release and shelf-life ranges acceptable?
  - Dissolution testing has not been included in the specification
  - The iron release test is for shelf-life only and will not be performed at release. Is there justification for this?

- The DMF

- A is proposed based on the additional stability data provided in a recent amendment. Is this acceptable? An acceptance criterion for iron release has not been established and is needed before an expiration dating period is granted. If dissolution testing is required, how is the absence of stability data for this parameter going to be handled?

- Should the annual stability commitment include from each of the sites?
Comments and Recommendations

The application is fileable -- see attached Filing Check List. Facilities have been entered into EES and the overall recommendation is currently “Pending”; the reviewer should confirm the completeness and accuracy of the entries. A categorical exclusion from environmental assessment has been requested. Methods validation will be not be initiated at this time since this not an NME. However, the reviewer should evaluate the non-traditional methods used for the drug substance and drug product to see if methods validation is called for. A single CMC reviewer is recommended since the drug product is a traditional chewable tablet composed of

Kasturi Srinivasachar
CMC Lead
Mar. 12, 2013

Ramesh Sood
Branch Chief
Mar. 12, 2013
The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies. On **initial** overview of the NDA application for filing:

### A. GENERAL

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<td>4. Has all information requested during the IND phase, and at the pre-NDA meetings been included?</td>
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### B. FACILITIES*

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<td>6. For a naturally-derived API only, are the facilities responsible for critical intermediate or crude API manufacturing, or performing upstream steps, specified in the application? If not, has a justification been provided for this omission? <strong>This question is not applicable for synthesized API.</strong></td>
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*For a naturally-derived API only, are the facilities responsible for critical intermediate or crude API manufacturing, or performing upstream steps, specified in the application? If not, has a justification been provided for this omission? **This question is not applicable for synthesized API.**

Reference ID: 3274822
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| 7. | Are drug substance manufacturing sites identified on FDA Form 356h or associated continuation sheet? For each site, does the application list:  
- Name of facility,  
- Full address of facility including street, city, state, country  
- FEI number for facility (if previously registered with FDA)  
- Full name and title, telephone, fax number and email for on-site contact person.  
- Is the manufacturing responsibility and function identified for each facility?, and  
- DMF number (if applicable) | X |
| 8. | Are drug product manufacturing sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:  
- Name of facility,  
- Full address of facility including street, city, state, country  
- FEI number for facility (if previously registered with FDA)  
- Full name and title, telephone, fax number and email for on-site contact person.  
- Is the manufacturing responsibility and function identified for each facility?, and  
- DMF number (if applicable) | X |
| 9. | Are additional manufacturing, packaging and control/test laboratory sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:  
- Name of facility,  
- Full address of facility including street, city, state, country  
- FEI number for facility (if previously registered with FDA)  
- Full name and title, telephone, fax number and email for on-site contact person.  
- Is the manufacturing responsibility and function identified for each facility?, and  
- DMF number (if applicable) | X |
10. Is a statement provided that all facilities are ready for GMP inspection at the time of submission? | X |  

* If any information regarding the facilities is omitted, this should be addressed ASAP with the applicant and can be a potential filing issue or a potential review issue.

### C. ENVIRONMENTAL ASSESSMENT

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Has an environmental assessment report or categorical exclusion been provided?</td>
<td>X</td>
<td></td>
<td>Categorical exclusion requested</td>
</tr>
</tbody>
</table>

### D. DRUG SUBSTANCE/ACTIVE PHARMACEUTICAL INGREDIENT (DS/API)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. Does the section contain a description of the DS manufacturing process?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Does the section contain identification and controls of critical steps and intermediates of the DS?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Does the section contain information regarding the characterization of the DS?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Does the section contain controls for the DS?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Has stability data and analysis been provided for the drug substance?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Does the application contain Quality by Design (QbD) information regarding the DS?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. Does the application contain Process Analytical Technology (PAT) information regarding the DS?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### E. DRUG PRODUCT (DP)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>19. Is there a description of manufacturing process and methods for DP production through finishing, including formulation, filling, labeling and packaging?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>20. Does the section contain identification and controls of critical steps and intermediates of the DP, including analytical procedures and method validation reports for assay and related substances if applicable?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>21. Is there a batch production record and a proposed master batch record?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>22. Has an investigational formulations section been provided? Is there adequate linkage between the investigational product and the proposed marketed product?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>23. Have any Comparability Protocols been requested?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>24. Does the section contain description of to-be-marketed container/closure system and presentations?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>25. Does the section contain controls of the final drug product?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>26. Has stability data and analysis been provided to support the requested expiration date?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>27. Does the application contain Quality by Design (QbD) information regarding the DP?</td>
<td></td>
<td>X</td>
<td>Some QbD elements provided</td>
</tr>
<tr>
<td>28. Does the application contain Process Analytical Technology (PAT) information regarding the DP?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

### F. METHODS VALIDATION (MV)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>29. Is there a methods validation package?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
### G. MICROBIOLOGY

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>30. If appropriate, is a separate microbiological section included assuring sterility of the drug product?</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
</tbody>
</table>

### H. MASTER FILES (DMF/MAF)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>31. Is information for critical DMF references (i.e., for drug substance and important packaging components for non-solid-oral drug products) complete?</td>
<td>X</td>
<td></td>
<td>LoAs to DMFs for ... provided</td>
</tr>
</tbody>
</table>

### I. LABELING

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>32. Has the draft package insert been provided?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33. Have the immediate container and carton labels been provided?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### J. FILING CONCLUSION

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>34. <strong>IS THE PRODUCT QUALITY AND BIOPHARMACEUTICS SECTIONS OF THE APPLICATION FILEABLE?</strong></td>
<td>X</td>
<td></td>
<td>Fileable for Product Quality. See Biopharmaceutics Filing Review for fileability of the Biopharm Section</td>
</tr>
<tr>
<td>35. If the NDA is not fileable from the product quality perspective, state the reasons and provide filing comments to be sent to the Applicant.</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>36. If the NDA is not fileable from the biopharmaceutics perspective, state the reasons and provide filing comments to be sent to the Applicant.</td>
<td></td>
<td></td>
<td>See Biopharm filing review</td>
</tr>
<tr>
<td>37. Are there any potential review issues to be forwarded to the Applicant for the 74-day letter?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reference ID: 3274822
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

application: NDA 205109/000
rg. C: 110
rio: 5
lamp Date: 01-FEB-2013
DUFA Date: 01-DEC-2013
ction Goal: 02-OCT-2013

Sponsor: VIFOR FRESENIUS
920 WINTER ST
WALTHAM, MA 02451

Brand Name: FERRIC OXYHYDROXIDE SUCROSTAMIX

Estab. Name: FERRIC OXYHYDROXIDE SUCROSTAMIX

Generic Name: FERRIC OXYHYDROXIDE SUCROSTAMIX

Product Number; Dosage Form; Ingredient; Strengths
001; TABLET; INGREDIENT TERM PENDING; 500MG

DA Contacts:
T. WONG
Prod Qual Reviewer
(HFD-810)
3017961608

D. MESMER
Product Quality PM
(HFD-800)
3017964023

A. PARK
Regulatory Project Mgr
3017961129

K. SRINIVASACHAR
Team Leader
3017961760

verall Recommendation: ACCEPTABLE on 03-APR-2013 by J. WILLIAMS () 3017964196
PENDING on 15-FEB-2013 by EES_PROD

establishment: CFN: [REDACTED] FEI: [REDACTED]

MF No:
responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
profile: TABLETS, PROMPT RELEASE
OAI Status: NONE
ast Milestone: OC RECOMMENDATION
ilestone Date: 04-MAR-2013
ecision: ACCEPTABLE
ason: DISTRICT RECOMMENDATION
FDA CDER LEG
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

establishment: CFN: 9613378  FEI: 3002808450
VIFOR INTERNATIONAL INC.
RESCHENSTRASSE 37
ST. GALLEN, SWITZERLAND CH-9001
MF No:
responsibilities:
DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE PACKAGER
DRUG SUBSTANCE RELEASE TESTER
DRUG SUBSTANCE STABILITY TESTER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER
profile:
CONTROL TESTING LABORATORIES "ALSO" (DRUGS)
OAI Status: NONE

1st Milestone:
OC RECOMMENDATION
19-FEB-2013
classification:
ACCEPTABLE
reason:
BASED ON PROFILE

establishment: CFN: 3009018997
VIFOR PHARMA
RTE DE MONCOR 10
VILLARS-SUR-GLJNE, FR, SWITZERLAND
MF No:
responsibilities:
FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER
profile:
TABLETS, PROMPT RELEASE
OAI Status: NONE
1st Milestone:
OC RECOMMENDATION
03-APR-2013
classification:
ACCEPTABLE
reason:
DISTRICT RECOMMENDATION
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KASTURI SRINIVASACHAR
03/12/2013

RAMESH K SOOD
03/12/2013