Correspondence Detail Report

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CBER 510(k), PMA, and PMS Submissions

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Applicant Firm: Fenwal Inc | **DCC Login ID:** 446481
Product: AAA unidentifiable product

Originator: FDA | **Correspondence DCC Login ID:**

Correspondence Type: Telecon | **Due Date Changed:** N

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Correspondence Purpose(s): Conversation record

Applicant Contact Person(s): Ms. Cheryl Chamberlain Roscher,

FDA Participant(s): Heather Erdman, OBRR APPROVED

Summary: PMC/PMR discussion

Comments: Fenwal BN080041/0 - PMC/PMR discussion:
10/15/09

FDA: Salim Haddad; Jaro Vostal; Heather Erdman

Fenwal: Cheryl Roscher; Jamie (Dir, of Clinical Affairs); Peyton; Brian Mc Mullen; Jason Davey (stat); Yvonne DiBartolo

FDA explained that FDAAA details post marketing requirements for FDA approved drugs and devices that it also established a formal process for whether a PM is justified and the type of the study; whether it meets PMR. During internal discussion with Division and Office Directors and also after discussion with the CBER Safety Working Group, the CBER SWG decided that a PMR, to track the AEs, and a PMC, to track the b(4) would be required. Both the PMC and PMR studies will need meaningful results and therefore will need to have a control arm.

Fenwal acknowledged this decision and discussed their thoughts on how the AEs could be tracked and how to mange a control arm. Fenwal explained that AE rates will differ from site to site, depending on their collection methodologies. It is difficult to develop a prospectively designed study. Fenwal suggested looking at site to site, under current reporting structures: make a conversion of platelets in plasma to platelets in InterSol, that would give them a control group (consecutive at the site) and it would not force sites to have a dual inventory. IRB approval would be required but an ICF would not be required. This would not be done at every site, only at specific sites (e.g. major oncology systems) that have a good reporting/ active surveillance transfusion system.
FDA inquired whether this would be active reporting with each transfusion; whether a form would be completed after each transfusion for both control and InterSol platelets.
Fenwal explained that many of these sites have an active surveillance in place and have their own forms that get completed on the floor and each time completed with an M.D. Fenwal recommended using the sites' own forms so that new terms would not have to be introduced. Fenwal clarified that this form is not

being completed for a 'no transfusion reaction'. Fenwal can capture the number of transfusions, and the number of reactions, when an AE occurs. FDA considered this passive reporting; Fenwal stated that these sites consider this active reporting. FDA noted that a consistent form would provide consistency in reporting. Fenwal explained that this is why they are only planning on working with sites that already have active reporting; they are aware that not all places have active reporting; a lot of these sites are accustomed to conducting clinical trials; they are accustomed to this level of active participation. Fenwal will provide these forms to FDA for review of what they are collecting to provide more assurance.

FDA asked how Fenwal would ensure reporting is equal at each center.
Fenwal explained that there will be differences at centers so they would like to look at the data at each site, not pool the data together. Percent AE rates can vary: 2% AE rate down to 0.8% AE. The reason for the differences is unknown at this time. Fenwal noted that there is appears to be a seasonal & month to month variation as well.
The sites say that it is patient dependent; if someone reacts they will continue to react; different parts of country/ seasonal. Therefore recommend evaluating this by site.

FDA recommended that they start with the same terminology. Fenwal stated that there are multiple terms but that it comes down to 'was there a transfusion reaction or not'. Fenwal explained that the sites have a time period cutoff; is it related to transfusion (e.g. within 6 hours). The MD will review chart to make assessment of relatedness.

Fenwal suggested that Phase 1 study consist of platelets in plasma and then switch to plasma in InterSol and then record in that group. The time period for each phase will depend on the sample size. If they collect for multiple months per phase this may balance out variation between patients.

FDA reminded them that a side by side comparison will require a large enough sample size to develop statistically significant results. Fenwal noted that this will be difficult because there are no specific transfusion reaction results. They could go with historical rates and note if it is statistically significant at each site: 10,000 at each site is a huge under taking, if at a rate of 0.8%. FDA suggested considering a non-inferiority study, not more than double the control. Fenwal explained that they were looking at it as observational study: how many transfusions and not state the sample size.

FDA explained that it is important to have a statistically significant sample size to derive meaningful results; a statistical plan should be included in the study.

Fenwal confirmed that they want to use the sites' existing forms and they will see if they add 'no reaction'. FDA confirmed that they want a data point for every transfusion that occurs, not only when a reaction occurs. FDA also confirmed that Fenwal understood the reporting requirements per FDAAA.

FDA stated that they expect to see the reaction rate per type and Fenwal explained that this gets down to the symptoms and that they can't do stats on all of the symptoms and that this increases the complexity of the study. Fenwal asked whether they could propose no MEDRA coding (coding dictionaries for coding AEs); just here are individual symptoms, verbatim. FDA thought this was OK.

Fenwal confirmed that they don't have to have the details worked out, just continue to negotiate with the protocol and the approval letter would need to have some information: final protocol submitted; estimated start and estimated duration

FDA asked whether an evaluation would be done on shipped products. Fenwal stated that they are still working out logistics, but that the shipments may be intrastate. Licensure may be an issue.

Fenwal requested to hold a face-to-face meeting to discuss this further and FDA requested that a first draft protocol be provided before this meeting. A face-to-face meeting could be held if really complex

Issue arise, although if the t-cons progress we should be fine.

PMC - b(4)
FDA explained that the 2nd study is a PM commitment, of the b(4) FDA will not be looking for a doubling, but that it is not more than 20% different to the control for b(4) Fenwal confirmed. They did look at the data across studies and saw no difference so they can consider the sample size.
Fenwal asked what the input is on multiplicity. FDA explained that there wasn't a statistician on the call. Fenwal will look into this.

The 510(k) should not be submitted until the NDA sterilization issue has been resolved. The 510(k) cannot be cleared without NDA approval but the NDA can be approved without 510(k) clearance, although the product would not be useful until the 510(k) was cleared.

Fenwal confirmed that b(4) is higher in PAS and that if all of the factors are the same then the b(4) level is higher by the amount of PAS delivered.