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Request for Comment--Docket No. 2003D-0504: Medical Devices; Guidance for Industry and FDA staff; Bundling Multiple Devices or Multiple Indications in a Single Submission

Dockets Management Branch (HFA-305)
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Office of Human Resources and Management Services
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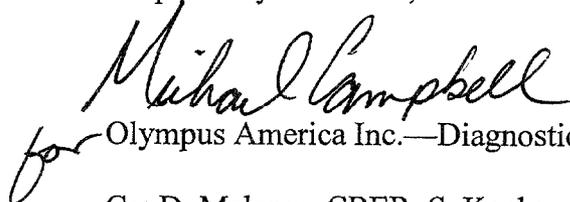
To Whom It May Concern:

Enclosed, please find comments for the above referenced docket number from Olympus America Inc. for the proposed guidance document regarding bundling of multiple devices in a single premarket submission.

The Olympus organization is a manufacturer of automated instruments used in blood establishments. Since 1988, Olympus has manufactured automated instruments used in blood establishments for ABO/Rh and infectious disease screening. Currently, more than 90% of North America's blood supply is tested on Olympus analyzer systems.

Olympus is concerned that the costs required to enter the ABO/Rh and antibody screening market will continue to limit the testing of the Nation's blood supply to the two companies that are currently providing those reagents. Within this guidance, we have presented further discussion of the concerns as well as suggestions for revisions to the fee determination process that will continue allow for diversity in this arena.

Respectfully submitted,


for Olympus America Inc.—Diagnostic Systems Group

Cc: D. Maloney-CBER, S. Kochman-CBER

2003D-0504

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Olympus America is a distributor of in vitro diagnostic devices for chemistry and blood bank applications. Our blood bank products are used for testing blood donors for ABO/Rh, syphilis and CMV. We are writing you to provide comments on the Medical Device User Fee and Modernization Act (MDUFMA) of 2002 as it affects the availability of blood group serology reagents in the United States.

As you may know, there are two main suppliers of blood group reagents in the United States, Ortho Clinical Diagnostics and Immucor/Gamma. In prior years, there have been many more suppliers, however market forces have caused all but these two to withdraw or to consolidate. The current lack of suppliers not only inhibits innovation among competitors; but it also threatens the safety of the blood supply and transfusion medicine in general. Should something happen to one supplier or one product line from one supplier, it is doubtful that the other would be able to make up the shortfall on short notice. This could leave some blood centers or hospitals unable to perform ABO and Rh typing, antibody screening and identification, or rare antigen typing.

While everyone in the blood bank industry agrees that new blood bank reagent suppliers are needed, there are significant obstacles to new entrants in this market. Regulatory hurdles in getting products approved and the subsequent FDA lot release requirements are huge as compared to in vitro diagnostic reagents reviewed by CDRH. To be competitive, the manufacturer must offer a full line of Blood Grouping Antisera, Reagent Red Cells and Anti-human globulin. This includes numerous rare antisera that can be considered "esoteric". The return on investment for most manufacturers takes a long time to realize.

While MDUFMA was long overdue in getting CDRH and CBER the necessary resources for timely device reviews, it has had a negative impact on the potential for new blood bank suppliers or even for new products from existing blood bank suppliers. While the recent guidance document "*Bundling Multiple Devices or Multiple Indications in a Single Submission*" offers potential for bundling some blood bank reagents, it does not go far enough. Immucor and Ortho blood group serology product offerings number in the hundreds. Even bundled, the number of Biologic License Applications for an entire product line would be cost-prohibitive for new market entrants. Since CBER does not have 180 Day Supplements or Real-time Supplements at reduced fees, modifications to existing products that require any clinical testing become Efficacy Supplements at the same full fee as Original BLAs. Due to the *in-vitro* diagnostic nature of these products,

clinical testing is always a requirement. Consequently, you will not see any enhancements or changes that require any clinical testing for existing licensed products.

In Europe, there continues to be six to seven blood bank suppliers. Several would be interested in having Olympus distribute their products in the United States. With our current involvement in the blood donor market, we are an obvious choice as a distributor. However, when we investigate the potential for these products versus the cost of bringing them to market, we cannot justify the expenditure. Paying millions of dollars in user fees is cost-prohibitive. Unfortunately, the customer and the US blood bank industry will be denied innovative products that are available elsewhere in the world.

Currently we are working with two manufacturers on an automated system for ABO/Rh and antibody screening. This application will be received at CBER within the next month. One manufacturer is responsible for the instrument, the antisera, the antihuman globulin and peripheral reagents. The other manufacturer, Medion Diagnostics, will supply the Reagent Red Cells for ABO and antibody screening. Medion's red cells are currently licensed in the US for manual use. The field trials are complete and this will be submitted as a bundled submission with one data packet for review. Olympus will serve as the US sponsor for this bundled submission. We have inquired about the bundling strategy for this submission and were surprised to learn that we may have to pay two BLA fees because reagents from two manufacturers were used. If we had used one manufacturer for all reagents, this would not have been the case although the amount of FDA reviewer time would remain constant regardless of whether there is one manufacturer involved or five. We understand that this has not been addressed in any of the guidance documents and request additional consideration of these types of circumstances.

We offer a few possible solutions that would allow new entrants to the blood bank market, would assure CBER of reasonable source of user fees, and would allow modifications to existing products.

Suggestion 1:

1. Follow the three broad classifications for BLAs as defined in 21 CFR 660 for Reagent Red Cells, Blood Grouping Antisera, and Anti-human Globulin. For each manufacturer, the first application in each of these categories would be an Original Biologic License Application at the full fee.
2. Each subsequent application under these general categories, whether a new antisera, new antisera bundle such as anti-K and anti-k, or a supplement requiring clinical data would be at the reduced fee.

Suggestion 2:

Allow a mechanism for reduced fees for orphan IVDs that take into account the economic potential of the product.

Suggestion 3:

Redefine the current BLA supplements to allow for reduced fee submissions similar to the fee schedule set up for PMAs.

Suggestion 4:

For complex manufacturing arrangements with multiple manufacturers of one system, the FDA should only require one fee for a submission that would otherwise qualify as bundled. The fee could be split among the manufacturers.

We believe that further refinement in the application and definitions of MDUFMA will not only allow the blood banks and transfusion services within the United States to have innovative, quality products, but also ensure a continuous supply of safe blood transfusions.

Thank you for the opportunity to express our concerns and recommendations.