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Statistical Review for 510(K) K033736, MERCI Retriever, Concentric Medical, Inc.

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## I. Introduction

The MERCI Retriever is intended for restoring blood flow in the neurovasculature by removing thrombus in patients experiencing an ischemic stroke. The MERCI Retriever is also indicated for use in the retrieval of foreign bodies misplaced during interventional radiological procedures in the neuro, peripheral and coronary vascular systems.

The MERCI Retriever consists of a Nitinol wire with a helical-shaped tip. The helix is covered with a platinum coil for radiopacity. The Nitinol core wire is coated with a hydrophilic coating, ending proximal to the helical-shaped tip. The tip of the MERCI Retriever has five loops, which are designed to capture thrombus from the neurovasculature and foreign bodies from the neurovasculature, peripheral vascular and coronary vascular systems. For both foreign body retrieval and thrombus removal, a microcatheter is positioned beyond the obstruction and the MERCI Retriever is deployed. The microcatheter and MERCI Retriever are pulled back to engage the foreign body or thrombus. All are then withdrawn from the body.

The MERCI Retriever is available in two configurations, MERCI Retriever X5 and MERCI Retriever X6. Both configurations are identical to the configurations available for the predicate device, Concentric Retriever (K030476). Concentric Retriever is indicated only for retrieving foreign body.

In this submission, the sponsor summarized data from a single-arm prospective study of 121 patients to demonstrate the safety and effectiveness of the device.

## II. Sponsor's Results and Reviewer's Comments

1. The current study did not include a concurrent control group. Further, note that the historical control successful revascularization proportion of 18% was taken as a fixed value not as a value from one single study. If the size of the control group can be obtained, this can be corrected.

In Table 4 (page 9) summary on patient baseline co-variables were listed, but no data on control patients was provided. If patient level data were available, imbalance in important co-variables can be adjusted.

2. As shown in Table 13 (page 20), a total of 1412 patients were screened in 25 centers, among these, 121 entered the study (Figure 1, page 7), seven patients were excluded due to reasons listed in Tables 14 and 15 (page 21). One hundred and fourteen patients in 17 centers were treated and included in the sponsor's analyses. (Table 16, page 22). Whether the exclusions were appropriate needs to be clinically determined.

3. Based on data of 114 patients pooled over 17 centers, the sponsor indicated that the proportion of patients who had successful revascularization was 61/114 or 54%. The proportion of success was statistically significantly higher than the 18% re-canalization rate experienced by the placebo group in the PROACT II study (the control as specified in the protocol), and the protocol specified minimum rate of 30%.

In Table 16, data on revascularization were provided by center, except in centers with small numbers

(three or less) of patients, the success proportions did not vary much. No statistically significant difference was found among centers in proportion of patients who experienced successful revascularization. Sponsor's pooled analysis is acceptable. Further, including the seven excluded patients, the proportion of patients who experienced successful revascularization was 50% (61/121) with 2-sided 95% confidence interval (41%, 60%). The proportion still was statistically significantly higher than the protocol specified minimum proportion of 30%, and the control proportion of 18%.

4. However, note that in Figure 7 (page 14), number of patients who had successful revascularization due to MERCI Retriever was **43**, not 61, please clarify.
5. To demonstrate that patient status at 30 day and 90 day follow-up depended on whether success was achieved in revascularization, the sponsor tabulated and graphed results of secondary outcomes such as 30-day and 90-day NIHSS (NIH stroke score), 30-day and 90-day Modified Rankin score and 90 day mortality by revascularization status (Tables 5 and Figure 3-7). The sponsor indicated that patients who had successful revascularization had statistically significantly better outcomes than patients who did not have successful revascularization in all five secondary endpoints (Figures 3-7). Further, in Table 6, 7 and 9 and 10, the secondary outcomes were listed by baseline NIHSS, patients with successful revascularization had better outcomes than patients who did not have successful revascularization.

Since patients with and without successful revascularization are likely to be different in baseline covariables (in addition to NIHSS), sponsor's above results could be confounded by these covariables. Data need to be reanalyzed via logistic regression adjusting for baseline covariables. Further, since revascularization due to MERCI Retriever is the subject treatment, only patients who had success outcome due to MERCI Retriever can be counted as successes, patients who had success outcome due to other subsequent treatment should be counted as failures.

6. Of the 114 treated patients, by 90 day follow-up there were a total of 43 death. Of the 61 patients who had successful revascularization, 15 patients were dead (25%), and of the 53 patients who did not have successful revascularization 28 were dead (53%). The details of all death were listed in Table 17. Additionally, there were a total of 20 serious adverse events, the details of these patients were listed in Table 18. Without information on control group, the safety of the device needs to be clinically evaluated.

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