The General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on Wednesday, April 27, 2011 to discuss, make recommendations, and vote on information related to the premarket approval application (PMA) supplement for Restylane, sponsored by Medicis Aesthetics, Inc.

Restylane is currently approved for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds. The sponsor is requesting an expanded indication, to include use of Restylane for augmentation of the lips.

With regard to Discussion Question 1, the Panel’s consensus was that Restylane as used for lip augmentation is generally safe, despite the large number of recorded adverse events. However, the Panel did have some concerns regarding serious adverse events, and they felt that this should be clearly listed on marketing and labeling information.

With regard to Discussion Question 2, the Panel’s consensus was that there was no significant concern regarding the lack of correlation between injected dose and change in lip fullness. The Panel did not feel that there would be a need to cite a maximum injectable dose; however, the Panel did have concerns regarding whether the product would have applicability to wide variety of physicians/situations, and that there should be a maximum injectable dose per lip. The Panel also felt that there should be training on application techniques and on that maximum injectable dose. The Division Director asked whether FDA should consider limiting to what was studied or use precautions regarding the safety and effectiveness above a certain amount. Dr. McGrath indicated that either could be an option but that the amount per lip should be stated.

With regard to Discussion Question 3, the Panel generally believes that no additional premarket studies are necessary regarding individuals with darker Fitzpatrick skin types, or in the male population. However, the Panel had serious concerns regarding the use of the product in a younger patient population (ages 18-22). Particular concerns mentioned included possible lip fibrosis with repeated injections, and other concerns related to the implications associated with use of the product for lip augmentation in younger individuals.

With regard to Discussion Question 4, the Panel generally believed that Restylane has been shown to be effective in lip augmentation. Regarding the second part of the question, there was significant variance among the Panel, since many thought that methods of assessing effectiveness are subjective. The majority of the Panel felt that the MLFS would be a good score to use for this purpose; other Panel members felt that patient GAIS and assessment by the treating physician would be useful methods.
With regard to Discussion Question 5, the majority of the Panel did not feel that a postmarket study should be required; however, several Panel members believed that a registry should be created to follow specific populations (particularly young adults aged 18-22). Some Panelists did feel that a postmarket study would be indicated for the young adult population. One Panel member recommended that a study be conducted in children, with appropriate followup time based upon their age at the time of initial treatment. Furthermore, the indication for use in children (e.g. for repair of physical issues with the lips) should be different from the indication for use for cosmetic effect.

With regard to Discussion Question 6, the Panel’s consensus was that the assessment of outcome was very subjective, and that more assessment tools would be better. The majority felt that the blinded evaluator would be a preferable tool, but a disadvantage would be that the blinded evaluator would not be aware of what the patient looked like before treatment. The patient’s perception of effectiveness was deemed very important by the Panel (GAIS). Regarding methods of assessing improvement, the Panel suggested photographic analysis, portrait or profile photography, quality of life metrics (with emphasis on comparison to baseline), and discrete anatomic outcomes. There were numerous comments on what constituted a clinically significant result, with particular emphasis on discrete anatomic measurements.

For Voting Question 1, regarding the safety of Restylane for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds, and for submucosal implantation for lip augmentation*, the Panel voted 6 Yes and zero No. There was one abstention.

For Voting Question 2, regarding the effectiveness of Restylane for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds, and for submucosal implantation for lip augmentation, the Panel voted the Panel voted 6 Yes and zero No. There was one abstention.

For Voting Question 3, which asked whether the benefits of Restylane for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds, and for submucosal implantation for lip augmentation, outweigh the risks of Restylane for mid-to-deep dermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds, and for submucosal implantation for lip augmentation, for purposes of approval, the Panel voted the Panel voted 6 Yes and zero No. There was one abstention.

The Panel member who abstained indicated that she would have voted Yes for all three voting questions, if the indications statement included an age restriction.

The meeting adjourned at 4:40 PM.

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*Note: For the three voting questions, the sponsor's proposed indication statement in its entirety was read into the record, as stated in the PMA supplement which was the subject for today's panel. However, the Panel was made aware that they were being asked to vote only on the safety, effectiveness and risk/benefit profile of the sponsor's proposed new indication for Restylane, which is "submucosal implantation for lip augmentation". 