AAOS
American Association of Orthopaedic Surgeons

May 3, 2024

Robert Califf, MD
Commissioner of Food and Drugs
Food and Drug Administration
Department of Health and Human Services

Submitted electronically.

Dear Commissioner Califf:

On behalf of the 39,000 orthopaedic surgeons and residents represented by the American Association of Orthopaedic Surgeons (AAOS), we are pleased to share our position on biological product regulation. AAOS views this as an opportunity to increase transparency and consumer education related to manufacturer reporting of these products. Critical to the AAOS commitment to the ethical use of orthobiologics among its members is transparent disclosure of the FDA status of the product in question.[1] This issue has been front and center to the AAOS since its letter to FDA in 2021.[2] In this letter, the FDA response was noted:

"Despite all of the FDA's efforts to engage industry, there continues to be broad marketing of these unapproved products for the treatment or cure of a wide range of diseases or medical conditions. Many of these unapproved products appear to be HCT/Ps that are regulated as drugs, devices and/or biological products subject to premarket approval requirements. The wide extent of the marketing of such unapproved products is evidenced by their inappropriate advertisement in various media and by the number of consumer complaints about them submitted to the FDA."[3]

To this end, AAOS strongly recommends that FDA continue its efforts to ethically regulate these products. Key to addressing this issue would be to require manufacturers to disclose the FDA status of their products on both their websites and press releases. A review of over 800 biologic products pending listing on the AAOS

[1] Orthobiologics (Regenerative Medicine) FAQ. Accessed at: https://orthoinfo.aaos.org/en/treatment/orthobiologics-faq/ Accessed on 8/28/23.

[2] AAOS letter to Janice Woodcock. Accessed at: https://www.aaos.org/globalassets/advocacy/issues/aaos-letter-to-the-fda-on-biologics-regulation_final_signed_111521.pdf. Accessed on 8/28/23.

[3] US Food and Drug Administration. (2021, April 21). Advancing the Development of Safe and Effective Regenerative Medicine Products. FDA Voices. Accessed at: https://www.fda.gov/news-events/fda-voices/advancing-development-safe-and-effective-regenerativemedicine-products.

Biologics Dashboard shows that virtually none of the manufacturers include this basic information either to patients or surgeons.

Many of the products are experimental, some are undergoing investigational research, and some are only CE marked in Europe, with no discussion of any ongoing approval processes. AAOS shares the following suggestions:

1) For those devices approved/cleared/or granted for use in the US, the status of the product should be clearly disclosed. This should include the 510(k), PMA, De Novo, or BLA number so that the appropriate FDA actions can be clearly confirmed by using the appropriate FDA website. If the manufacturer has clear documentation that the product is categorized as a 361 HCT/P 21 per CFR 1271.10(a) and therefore is subject only to regulation under section 361 of the Public Health Service Act (PHS Act) this should also be defined, with a link to the appropriate confirmation(s).[4] The current process involves researching numerous FDA databases, which are frequently incomplete or inconsistent, especially as both the manufacturers and product names can change numerous times during the life cycle of the product, further complicated by the fact that FDA does not regulate 361 HCT/P products.

2) For investigational products, the reader of the website should be directed to the study listed on ClinicalTrials.gov so that current information regarding the progress of the device in this clinical research can be identified. This would have the additional advantage of improving recruitment for legitimate researchers employing studies utilizing these devices.

3) If neither of these is true, it should be clearly stated on the website "Not available for use in the US." Failure to disclose this should be construed as an immediate flag to AAOS membership that the product in question cannot be legally applied to patients.

Full, transparent disclosure is in the best interest of patients, surgeons and in the end, manufacturers. Particularly for those who have undergone tremendous time and effort to establish the legitimacy of their products. The genuine manufacturers of these products should have no issue with these basic disclosure requirements. Yet, the pressure applied to the illegitimate suppliers of unapproved biologics would be significant.[5]

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[4] Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products. Accessed at: (HCT/Ps) https://www.fda.gov/media/70689/download

[5] Chu CR, Rodeo S, Bhutani N, Goodrich LR, Huard J, Irrgang J, LaPrade RF, Lattermann C, Lu Y, Mandelbaum B, Mao J, McIntyre L, Mishra A, Muschler GF, Piuzzi NS, Potter H, Spindler K, Tokish JM, Tuan R, Zaslav K, Maloney W. Optimizing Clinical Use of Biologics in Orthopaedic Surgery: Consensus Recommendations From the 2018 AAOS/NIH U-13

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Thank you for your time and attention to the concerns and suggestions of the American Association of Orthopaedic Surgeons (AAOS). We look forward to working closely with the FDA on further improving the healthcare system and enhancing the care of musculoskeletal patients in the United States. Should you have questions on any of the above comments, please do not hesitate to contact Shreyasi Deb, PhD, MBA, AAOS Office of Government Relations at deb@aaos.org.

Sincerely,

Paul Tornetta III, MD, PhD, FAAOS
AAOS President

cc: Annunziato Amendola, MD, FAAOS, First Vice-President, AAOS
Wilford K. Gibson, MD, FAAOS, Second Vice-President, AAOS
Thomas E. Arend, Jr., Esq., CAE, CEO, AAOS
Nathan Glusenkamp, Chief Quality and Registries Officer, AAOS
Lori Shoaf, JD, MA, Vice-President, Office of Government Relations, AAOS
Jason L. Dragoo, MD, FAAOS, Chair, AAOS Devices, Biologics and Technology Committee

Jeffrey Shuren, MD, JD, Director of the Center for Devices and Radiological Health, FDA
CAPT Raquel Peat, Ph.D., Office Director, Office of Health Technology 6 (OHT 6: Orthopedic Devices), FDA

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