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Dear Potential ScolioScore™ User:

Axial Biotech appreciates your concern about the FDA status for the ScolioScore™ AIS Predictive Assay and understands that there has been a lot of conflicting information about the status of Laboratory Developed Tests. The ScolioScore™ assay is legally marketed as an in-house or laboratory-developed test regulated under the federal Clinical Laboratory Improvement Amendments (CLIA). No pre-market clearance (under Federal Food, Drug and Cosmetic Act [FFDCA] § 510(k)) or pre-market approval (PMA) by the Food and Drug Administration (FDA) is required for this assay to be lawfully marketed at this time.

The ScolioScore™ assay is an in-house or laboratory-developed test procedure, meaning that the assay was developed by a laboratory for that laboratory's own use in testing and reporting results on specimens referred to the laboratory. In the case of ScolioScore™, the assay was developed and is performed solely by Axial Biotech, Inc. (Axial) a licensed and CLIA-certified, clinical laboratory located in Salt Lake City, Utah. Axial was required, under CLIA, to conduct studies to establish the performance specifications for ScolioScore™ prior to being able to offer the test commercially.¹ In addition, Axial must comply with regulatory oversight requirements under CLIA and Utah law, including regular inspections and compliance with regulations covering quality systems and personnel standards.

The regulatory status of in-house tests, like ScolioScore™, under the FFDCA is unclear. Although FDA has maintained that these tests may be medical devices as that term is defined under the FFDCA,² this issue has not been addressed by the courts. Whether or not the courts would agree with FDA that in-house tests are medical devices under the FFDCA, FDA has exercised enforcement discretion not to require pre-market clearance (510(k)) or pre-market approval for these tests. In the preamble to its 1997 regulation on analyte-specific reagents—components of certain in-house tests, FDA explained its rationale for not requiring pre-market clearance or approval for these tests:

FDA has considered . . . and appreciates the concerns raised about the development of in-house tests and the current marketing of test services based on tests that have not been reviewed independently for safety and effectiveness. FDA believes that clinical

¹ *Establishment of performance specifications.* Each laboratory that modifies an FDA-cleared or approved test system, or **introduces a test system not subject to FDA clearance or approval (including methods developed in-house and standardized methods such as text book procedures)**, or uses a test system in which performance specifications are not provided by the manufacturer must, before reporting patient test results, establish for each test system the performance specifications for the following performance characteristics, as applicable: (i) Accuracy. (ii) Precision. (iii) Analytical sensitivity. (iv) Analytical specificity to include interfering substances. (v) Reportable range of test results for the test system. (vi) Reference intervals (normal values). (vii) Any other performance characteristic required for test performance. (42 C.F.R. § 493.1253(b)(2))(Emphasis added).

² Under FFDCA § 201(h), "The term 'device' . . . means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals . . ." (21 USC § 321(h))(N.B.: Although this definition would cover equipment and supplies laboratories may purchase to perform clinical laboratory tests, the definition does not describe a laboratory procedure that uses such equipment or supplies).

laboratories that develop such tests are acting as manufacturers of medical devices and are subject to FDA jurisdiction under the act. However, FDA recognizes that the use of in-house developed tests has contributed to enhanced standards of medical care in many circumstances and that significant regulatory changes in this area could have negative effects on the public health. For these reasons, FDA declines to accept the suggestion that all in-house developed tests be classified as class II or III medical devices. 62 Fed. Reg. 62,243, 62,249 (Nov. 21, 1997)

Under this FDA policy, in-house or laboratory-developed tests, like Scoliscore™, have not been required to undergo pre-market clearance or approval in order for these tests to enter and remain on the market lawfully.

Recently, FDA has proposed new enforcement policy under which certain in-house tests would be subject to FDA regulatory requirements. FDA has described the scope of tests that may be subject to this new policy as “in vitro diagnostic multivariate index assays” (IVDMIA).³ Importantly, FDA has proposed this new policy under two versions of a **draft guidance** document. This guidance document has not been finalized, however, and FDA has not taken any enforcement action against laboratories that currently market tests that may fit under the Agency’s new IVDMIA category of in-house tests. In fact, the latest draft guidance indicates that, following finalization of a guidance document, FDA would continue to exercise enforcement discretion for currently marketed IVDMIA for up to 18 months.⁴ Based on this information, Axial remains comfortable that this product is lawfully marketed at this time.

If FDA finalizes new rules or enforcement policies requiring FDA pre-market clearance or approval for Scoliscore™, Axial will comply with those requirements

We trust this information will address the concern you raised about the lawful marketing and use of the Scoliscore™ assay.

Sincerely yours,



Rina Wolf
Vice President, Reimbursement and Regulatory Affairs
Axial Biotech, Inc.

³ Draft Guidance for Industry, Clinical Laboratories, and FDA Staff In Vitro Diagnostic Multivariate Index Assays. First draft issued September 7, 2006; revised draft issued July 26, 2007.

⁴ For 12 months following publication of the final guidance document, FDA intends to exercise enforcement discretion with respect to all regulatory requirements for currently marketed, laboratory-developed IVDMIA. FDA intends to exercise enforcement discretion for an additional 6 months for currently marketed, laboratory-developed IVDMIA if the manufacturer submits a 510(k) or PMA within the initial 12 month period following publication of the final guidance. *Id.*