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FEB - 2 2000

WARNING LETTER

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

VIA FEDERAL EXPRESS
VIA FACSIMILE

Vysis, Inc.
John L. Bishop
President and CEO
3100 Woodstock Drive
Downers Grove, Illinois 60515-5400

Dear Mr. Bishop:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has reviewed press releases distributed by Vysis Inc. (Vysis) and the Vysis Internet site found at www.vysis.com. The product referenced in this material is the AneuVysion™ Multicolor Probe Panel (AneuVysion™ Assay). The AneuVysion™ Assay is a device as defined within the meaning of section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The intended use of the AneuVysion™ Assay that was cleared in Vysis' 510(k) premarket notification submission designated 972200 was as follows. "The AneuVysion™ (CEP 18, X, Y-alpha satellite, LSI 13 and 21) Multicolor Probe Panel is intended to use CEP 18/X/Y probe to detect alpha satellite sequences in the centromere regions of chromosomes 18, X, and Y, and LSI 13/21 probe to detect the 13q14 region and the 21q22.13 to 21q22.2 region. The AneuVysion™ kit is indicated for use as an adjunct to standard cytogenetic metaphase analysis for identifying and enumerating chromosomes 13,18,21, X, and Y via fluorescence in situ hybridization (FISH) in metaphase cells and interphase nuclei obtained from uncultured amniotic fluid in subjects with presumed high risk pregnancies. It is not intended to be used as a stand-alone Assay for test reporting. FISH results are intended to be reported and interpreted only in conjunction with results of standard cytogenetic analysis, performed concurrently, utilizing the same patient specimen. FISH results should not be reported prior to standard cytogenetic results except in instances where reporting of FISH results alone is medically indicated or standard cytogenetic results are not available, e.g., culture failure. Reporting and interpretation of FISH should be consistent with professional standards of practice [1]. This device is intended for use only with amniocyte cells; it is not intended for and has not been validated for use with other test matrices. This FISH Assay will not detect the presence of structural chromosome abnormalities frequently associated with birth defects. This FISH Assay will be performed in cytogenetics laboratories."

Although the AneuVysion™ Assay was cleared as an adjunct to standard cytogenetic test, the agency has reviewed several promotional pieces that make certain representations and statements that result in the AneuVysion™ Assay being marketed as a stand alone test.

A press release dated September 16, 1999, entitled "Study Reports 24-Hour Prenatal FISH Test 100% Accurate in the Management of High-Risk Pregnancies." The press release states "our comprehensive study showed that the more rapid fluorescence in situ hybridization (FISH) results were in complete agreement for all analyzable disorders with standard cytogenetics, a time consuming procedure lending to a distressful wait. The timely results from AneuVysion™ Assay can alleviate this anxiety within 24 hours providing immediate relief to the pregnant woman and her family." Vysis' claim of complete agreement with standard cytogenetic tests, statements that the standard cytogenetic test is time consuming and distressful, and statements that the AneuVysion™ Assay can offer immediate relief to the patient are inconsistent with the cleared intended use and imply that the AneuVysion™ Assay can be used as a stand alone test.

Similar claims are also made in another press release dated January 18, 2000. The title of the press release is "Expectant Mothers Say Vysis' 24-Hour Prenatal Chromosome Test Reduces Anxiety." The following testimonial is representative of the misleading claims found in the press release. "I knew about the AneuVysion Assay and asked my doctor to make sure the lab ran the test so I wouldn't have to wait for two to three weeks to get my results. I received the results the next day and was then able to share the good news with my family and enjoy the holidays."

Vysis' Internet site entitled "FACTS: Down Syndrome and Other Chromosome Aneuploidies," at www.vysis.com/hm_crc_prent_AnVys_downs.asp describes the AneuVysion™ Assay as "provid[ing] important information about the fetus in a timely manner with the assurance of having obtained rapid, reliable test results." Similar representations can be found at www.vysis.com/hm_crc_prent_AnVys_Patient.asp on a web page entitled, "AneuVysion™ Prenatal Genetic Testing Patient Guide-Rapid Answers to Uncertainty Improvements in Prenatal Management." Both the description and the title of the web page are misleading in that they suggest that the patient, in making her final decision, does not have to wait for the standard cytogenetic results. Although the latter material is followed by an asterisk that refers the reader to the intended use statement, the constant use of words and phrases such as "rapid" and "within 24 hours" creates the overall impression that results of the AneuVysion™ Assay may be considered final.

An additional instance of Vysis' promotion of its AneuVysion™ Assay as a stand alone test is also found on the same web page entitled "FACTS: Down Syndrome and other Chromosome Aneuploidies." The description of the assay on this page as one that provides a "rapid, reliable test result" under a heading regarding Down Syndrome, implies that the assay can be used independently to detect birth defects such as Down syndrome.

Vysis' promotion of its device both in the aforementioned press release and on its Internet site as one that is 100% accurate, having no false-positives or false-negatives is also indicative of promoting the device as a stand alone test. Please provide us with the evidence you are using to support this 100% accuracy claim.

Although physicians may decide to report the results of the AneuVysion™ Assay, to their patients, prior to the completion of standard cytogenetic test, Vysis goes beyond its cleared intended use by representing the AneuVysion™ Assay as error free and implying that it can be used as a replacement for the standard cytogenetic test. The agency also objects to your use of descriptions and statements that imply that your Assay has the ability to diagnose birth defects.

Claims that imply that the AneuVysion™ Assay can be used as a stand alone test and that the test has the ability to diagnose birth defects have misbranded and adulterated the device within the meanings of sections 502(o) and 501 (f)(1)(B) of the Act. The AneuVysion™ Assay is misbranded because a notice or other information respecting the device was not provided to the FDA as required by section 510(k) and it has not been found to be substantially equivalent to a predicate device for the uses claimed. The device is adulterated because it is a class III device under section 513(f) and does not have approved applications for premarket approval in effect pursuant to section 515(a) or approved applications for investigational device exemptions under section 520(g).

FDA's regulations at 21 CFR 801.4 provide that the term "intended uses" of a device refers to the objective intent of the persons legally responsible for the labeling of a device. That intent may be shown by labeling claims or advertising matter or oral or written statements by such persons or their representatives. Making claims that your device can be used as a stand alone test or that the test has the ability to diagnose birth defects, changes the intended use for which the AneuVysion™ Assay was cleared. Pursuant to section 510(k) of the Act and as provided in 21 CFR 807.81(a)(3)(ii), claims that constitute a major change in the cleared intended use of a device require the submission of premarket notification to FDA.

The specific violations in this letter may represent practices used in other promotional or advertising materials used by your firm. You are responsible for investigating and reviewing these materials to ensure compliance with applicable regulations.

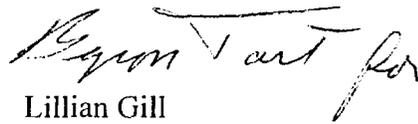
You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by FDA without further notice. These actions include, but are not limited to, seizure, injunctions and/or civil penalties. This letter is not intended to be an all-inclusive list of deficiencies associated with the AneuVysion™ Assay.

Please notify this office in writing within 15 working days of your receipt of this letter of the specific steps you have taken to correct the cited violations. Your response should include steps being taken to address misleading information currently in the marketplace and actions to prevent similar violations in the future. If corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Send your response to Terri Garvin, Regulatory Counsel, Promotion and Advertising Policy Staff, Office of Compliance (HFZ-302), Center for Devices and Radiological Health, 2098 Gaither Road, Rockville, Maryland 20850.

A copy of this letter is being sent to FDA's Los Angeles District Office. Please send a copy of your response to the District Director, Los Angeles District Office (HFR-PA-240), 19900 MacArthur Boulevard, Suite 300, Irvine, California 92715.

Sincerely,

A handwritten signature in cursive script, appearing to read "Lillian Gill", written in black ink.

Lillian Gill
Director
Office of Compliance
Center for Devices and
Radiological Health

Draft: TGarvin: 11/4/99
Consult:12/15/99:P.Maxim
Consult:1/4/99:J.Dawson
Reviewed:1/5/00:B.Tart
Revised:1/6/00
Reviewed:1/12/00:B.Tart
Revised:1/13/00
Reviewed:1/20/00
Revised:1/21/00
Revised:1/27/00
Reviewed:1/28/00
Revised:1/28/00
Reviewed:2/20/00:P.Maxim
Final: 2/2/00
Bcc:
HFA-224
HFZ-302
HFZ-305
HFZ-1(D.W. Feigal)
HFZ-300(L. Gill)
HFZ-440(P.Maxim)
HFR-PA-240
HFC-210 (D. Carroll)
HFC-130
HFC-230
HFC-240 (Comstat)
HFZ-306 (C. Condon)
HFI-35
HFZ-305 (L. Silver)
HFC-135
HFI-20