DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Food and Drug Administration
10903 New Hampshire Avenue
Building 66

TO: Stephen F. Kingsmore, Director
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FROM: E. David Litwack, PhD
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301-796-6697

RE: Q140271
DEVICE: Illumina HiSeq 2000/2500, NextSeq 500
DATED: March 4, 2014
RECEIVED: March 6, 2014

DATE: May 8, 2014

Dear Dr. Kingsmore,

Thank you for participating in our telecon last week. As stated during the call, we have discussed internally whether your proposed study will require an IDE. Based on the information provided in your presubmission and during the telecon, FDA has determined that your proposed clinical investigation is a nonsignificant risk (NSR) device study and you do not need to submit an IDE application for this investigation. This nonsignificant risk assessment is based on the following rationale: 1) Although you may return investigational test results to the treating physician that may influence important treatment decisions prior to their confirmation, this risk is lessened because the study population is critically ill, unlikely to be diagnosed quickly by other mechanisms, and suffers from a high mortality rate, 2) the treating physician can apply clinical judgment on whether treatment based on a preliminary, investigational result is warranted for a given patient, including considering the potential

risk(s) the patient may incur given the nature/severity of the treatment, and 3) all returned investigational test results will ultimately be confirmed.

We have provided some information below regarding NSR studies that may be helpful to you. If you have any additional questions regarding this risk assessment or the information below, we are happy to set up a follow-up call. Please contact me at (301) 796-6697 or at ernest.litwack@fda.hhs.gov.

NSR Study Information

An IDE application is not required to be submitted to, or approved by, FDA for a NSR study. A NSR study is, however, subject to the abbreviated requirements described in § 812.2(b) of the IDE regulation. The abbreviated requirements stipulate that the sponsor of the investigation must label the device in accordance with § 812.5; obtain institutional review board approval of the investigation as a NSR study; ensure that each investigator obtains informed consent from each subject under the investigator's care; comply with the monitoring requirements of § 812.46; maintain records required under § 812.140(b)(4) and (5) and file the reports required under § 812.150(b)(1) through (3) and (5) through (10); and ensure that participating investigators maintain the records required by § 812.140(a)(3)(i) and file the reports required under § 812.150(a)(1), (2), (5) and (7).

Under the abbreviated IDE requirements, a sponsor must also comply with the prohibitions against promotion and other practices as identified in § 812.7. According to this section of the regulation, the sponsor of a NSR study, investigator, or any person acting for or on behalf of the sponsor or investigator is prohibited from promoting or test marketing the investigational device until after FDA has approved the device for commercial distribution; commercializing the device by charging a price greater than that necessary to recover the cost of manufacture, research, development, and handling; unduly prolonging the investigation; and representing the investigational device as being safe or effective for the purposes for which it is being investigated.

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Please note that, if in the future you submit an application under sections 505, 515, or 520(m) of the FDCA (21 USC §§ 355, 360(e), or 360(j)(m)), or under section 351 of the PHS Act (21 U.S.C. § 262), or you submit a report under section 510(k) of the FDCA (21 USC § 360(k)), the application or submission must be accompanied by a certification that all applicable requirements of section 402(j) of the PHS Act (42 USC § 282(j)) have been met. Where available, such certification must include the appropriate National Clinical Trial (NCT) control numbers (42 USC § 282(j)(5)(B)). Additional information regarding the certification is available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM164819.pdf . Additional information regarding Title VIII of FDAAA is available at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html. Additional information on registering your clinical trial(s) is available at the Protocol Registration System website (http://prsinfo.clinicaltrials.gov/).