Hans G. Franke
President and
Chief Executive Officer

May 1, 2009

VIA ELECTRONIC MAIL

Stewart Marsden
Corporate Business Development
BD
stewart_marsden@bd.com

Re: Re-Introduction to Sierra Molecular AssayAssure® Sample Stabilization Platform

Dear Stewart:

Thank you for the opportunity to re-introduce Sierra Molecular to BD.

In the two years that have elapsed since Health Advances brought our work to BD's attention, Sierra Molecular has both improved its core nucleic acid stabilization technology (called AssayAssure®) and developed important new products focusing on mRNA retrieval, flow cytometry, and multiplex applications. In 2007, we gave you a glimpse of our technology as a work-in-progress. Today, we ask you to evaluate a platform technology and a pipeline of products that can significantly augment and enhance many aspects of BD's commercial offerings.

Robust Technical Platform, Yielding a Pipeline of Patent-Protected Products

The purpose of this correspondence is to provide you with a summary of **what is new** at Sierra Molecular; but perhaps it is prudent to start with a general overview of the AssayAssure® technology.

Sierra Molecular's AssayAssure® products stabilize human, bacterial, and viral cells and intracellular targets over extended time periods without freezing or refrigeration. This enables extraction of labile RNA and DNA from bacteria, viruses, and parasitic pathogens for diagnostic assays, even in extremely low target samples and highly inhibitory sample matrices. The AssayAssure® platform has spawned two families of formulations. The Hemolock® formulations preserve high quantity, high quality mRNA in whole blood, even after seven days at room temperature. Moreover, it stabilizes blood cells for non-molecular assays, such as flow cytometry and permits standard blood chemistry testing and classical microbiology. The Genelock® formulations address the variability of non-blood matrices. (Supporting data for these claims are available under an NDA.)

The AssayAssure® chemistries stabilize targets and improve the sensitivity and specificity of assays for four principal reasons:

- They dramatically extend cell viability at room temperature in matrices such as urine and blood by slowing cellular metabolism.
- They retard the reproduction and lysis of bacteria, whose enzymes are highly destructive of targets.
- They neutralize the metaloproteases within the sample matrices, which have a profound inhibitory effect on target amplification.
- They create significant interference with nuclease and protease activity, helping to preserve

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the most labile nucleic acids.

From the AssayAssure® platform (see Appendix A), we have derived a pipeline of discrete products (Appendix B), at different stages of development, applicable to specific clinical, research, and forensic needs.

We understand that BD has twice conducted tests on "Sierra" products. The first was on a discontinued gonorrhea assay called Gonostat, a product completely unrelated to the AssayAssure® technologies and never manufactured by Sierra Molecular. Gonostat was last sold in 2003, by a company called Sierra Diagnostics. The other test, which occurred in late 2003 or early 2004, focused on the earliest version of what would become the AssayAssure® chemistries, then called DNA/RNA Protect, for CT/GC urine samples. We have good reason to believe that this later experimentation demonstrated considerable success. You will note from Appendix A that Sierra Molecular has since expanded its pipeline with five additional formulations across two generations of chemistries.

Sierra Molecular's R&D Program: 2007 - 2009

Sierra Molecular has invested nearly $3 million to create and leverage a product development network of advisors, consultants, and laboratories. Since 2007, we have:

- **Developed New Whole Blood Stabilization Products.** We worked in close collaboration with Dr. Carl Wittwer (principle inventor of the Roche LightCycler qPCR, Professor of Pathology at the University of Utah Medical School, and Director of Advanced Studies at ARUP Laboratories) to develop new tools for stabilizing molecular targets and lymphocyte cell-surface antigens in unrefrigerated whole blood samples. Our development criteria involved preservation of white cells through metabolic enhancement, little or no hemolysis, stabilization of cell-surface proteins, high quality and yield of leukocyte mRNA, and high fidelity in gene expression patterns. The development team worked through numerous variations in the core components of our chemistries, modulations in the molar strengths of the chemistry, and combinations of protease inhibitors to develop products:

  1. *To stabilize leukocyte mRNA* through 120 hours by means of cell stabilization and sample matrix detoxification, rather than by lysis and precipitation. This presents a whole blood stabilization tool yielding optimal mRNA extraction for amplified molecular assays and microarrays. Sierra Molecular's Hemolock® offers significant complementary advantages to PAXgene™, since it (a) takes a different approach to RNA acquisition: stabilization vs. precipitation, (b) requires no proprietary purification kit, (c) is easier to use, and (d) delivers large quantities of high quality target.

  2. *To stabilize human lymphocytes* in whole blood samples through 120 hours for use in flow cytometry subset panels. This provides the basis of both a standard collection tool for flow cytometry as well as the potential to improve mid-stream workflow logistics.

  3. *To preserve viral and bacterial nucleic acids* in unfractionated, unrefrigerated blood for more than a week.

  4. *To perform all of the above functions from a single whole blood sample*. This combination permits valuable cross-platform diagnostic opportunities, such as a universal HIV tube, from which aged, unrefrigerated whole blood could yield primary detection, viral subtyping, viral load, and immunological status. Pharmaceutical developers, for example, would have the opportunity to do simultaneous gene expression studies and immunophenotyping.

- **Formulated a Specific Product for Multiplex Applications.** We have created a special formulation of Genelock®, Genelock Multiplex®, which in addition to preserving labile, low

prevalence targets, helps to optimize amplification where annealing times, temperatures, and primer sequences are compromised in co-reaction assays. This multiplex qPCR solution is currently in use in NIH-funded Human Microbiome Project research at LSU.

- **Launched a Patented Swab/Sponge Collection Kit**. We launched a unique sample collection kit, utilizing a chemistry-impregnated in-tube sponge, available in any of our Genelock® formulations. This product is different from standard "dry" swab kits in that, after the sample is taken and the swab is sheathed in its tube, the Genelock® chemistry is released into the swab bud to stabilize the sample. This collection device has been validated in CDC/WHO HIV studies, an FDA clinical trial of HSV I-II vaccine, and various environmental testing applications.

- **Demonstrated the Mechanism of Action in AssayAssure® Chemistries.** We have experimental data to show that AssayAssure® formulations operate by means of "biostasis" – retarding cellular metabolism and preserving cell viability – rather than by fixation. In experiments conducted by SNBL Laboratories, unrefrigerated whole blood samples showed little or no hemolysis and exceptional white cell viability (as determined by absolute CD45 counts, propidium iodide staining, and CBC) through 168 hours. We have also demonstrated remarkable bacteriostasis, yielding stable populations with sufficient vital resiliency that the bacteria can be cultured more than one week after the samples were drawn.

- **Collaborated on Novel Applications of Nucleic Acid Stabilization.** We have leveraged the AssayAssure® platform to formulate new chemistries for academic researchers, public health institutions, and other laboratories to address novel, complex, or otherwise unmet challenges in nucleic acid stabilization. This included amplification of gene transcripts from prostate cancer cells in urine samples for studies at the University of Michigan, Harvard Medical School, and the Fred Hutchinson Cancer Institute. It has also enabled the isolation of highly labile rickettsia and coxiella RNA from within mammalian host cells, for PCR, qPCR, and microarray analysis.

Other Accomplishments Since 2007

In addition to our active R&D program Sierra is manufacturing more than 250,000 tubes of product per year, in strict compliance with FDA regulations, to meet the demands of clinical and research customers. We have also:

- **Marshaled Diverse Scientific Evidence of the Effectiveness of Our Chemistries.** With the help of Health Advances, we have aggregated and vetted experiments and validation studies conducted over seven years from over 60 independent institutions. We have synthesized this data into an evidence-based demonstration of the effectiveness of AssayAssure® over a broad range of applications.

- **Consolidated Our Intellectual Property Portfolio.** We have continued to add to our patent portfolio, which now includes a total of 16 patent filings (one granted, 6 provisional, 5 non-provisional, and 4 international under PCT), creating a formidable barrier to entry for potential competitors. We have received both Freedom to Operate and Freedom from Domination Opinions from patent counsel with respect to the core AssayAssure® technology.

Incorporation of Sierra Molecular Technologies into BD Product Lines

We believe that Sierra Molecular's core technology and diversified product offerings can add value over a broad spectrum of BD's present and future commercial interests. We see performance-enhancing sample acquisition technology as an integrated front-end disposable for instrumentation and assay customers, as a value-add to the Vacutainer® tube business, as the tool-of-choice for food safety and bio-hazard testing, and as an enabling process for genomic pharmaceutical development and complex research applications. AssayAssure® tools also have the promise of being game-changers in global health applications, paring expense and easing time constraints on clinic-to-lab

logistics, creating powerful new multi-platform diagnostics for HIV and other pandemic infectious diseases, and enabling far-reaching third-world epidemiology.

Obviously, Sierra Molecular does not have an insider's understanding of BD's strategies and needs; but from our vantage point, here are some of the possible applications:

- **BD Biosciences:**
    - Genelock® for urine-based research applications, including prostate and bladder cancer diagnostics
    - Genelock® and Genelock® Multiplex for bacterial genomics and antibiotic development research applications
    - Hemolock® for pharmaceutical development, in medical genomics and combination genomics-immunophenotyping applications
    - Hemolock® for HIV, HCV, HPV and other viral genomic research, using stabilized, unfractionated, unfrozen whole blood samples rather than frozen plasma

- **BD Diagnostics**
    - Diagnostic Systems
        - Genelock® for the stabilization of pathogens in urine for standard molecular STD testing applications
        - Genelock® Multiplex for the stabilization of pathogens in urine for next-generation, broad-panel STD testing
        - Genelock® and Genelock® Multiplex for next generation, noninvasive, urine-based primary diagnosis of prostate and bladder cancer
    - Preanalytical Systems
        - Hemolock® for extended stabilization of lymphocytes in whole blood for flow cytometry
        - Hemolock® HIV Tube for multi-platform testing for primary detection, viral load, viral genotyping, and immunophenotyping
        - Genelock® as a universal stabilizer for urine cups
        - Genelock® Swab/Sponge Kits for bacterial and viral sample collection in non-blood, non-urine matrices
        - Genelock® Environmental and Genelock® Swab/Sponge Kits for earth science, food testing, bio-hazard, and other environmental applications

- **Global Health:**
    - Hemolock® HIV Tube for multi-platform testing for primary detection, viral load, viral genotyping, and immunophenotyping, in furtherance of WHO objectives for universal HIV testing in Africa and other developing countries
    - Hemolock® as the next generation Vacutainer® tube additive for immunophenotyping of HIV patients, moving from CD4-only assessment to capability for critical CD4:CD8 ratios and complete lymphocyte subset panels
    - Combo HIV Tube for whole blood tube testing to be used for HIV applications which allows for both flow cytometry (CD4:CD8) and molecular testing (primary detection, viral subtyping, and viral load)
    - Multi-test urine cup
    - Genelock® Swab/Sponge Kits for bacterial and viral STDs

- **PreAnalytiX:**
    - Hemolock® for non-precipitating, extended stabilization of mRNA in unrefrigerated whole blood, complementary to PAXgene™ as outlined in Sierra Molecular's R&D Program: 2007 – 2009 above

Next Steps

We believe our development activity over the past two years, combined with the ongoing success of our core technology in research labs and in clinical applications, provide BD with a valuable opportunity for acquisition or partnership. The brief summary in this correspondence is not meant to replace the kind of in-depth scientific data review and free-flowing face-to-face discussions that can occur under NDA. Nor can it supplant hands-on testing of our products in your labs, which can occur under the defined protocols of an MTA. This is simply a first step, down what we believe, will be a path of mutually advantageous dialogue. We want to provide information in a way that is directly responsive to BD's commercial priorities.

We look forward to further discussions.

Very truly yours,

Hans G. Franke
President and CEO

HGF:mbj

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Appendix A

Sierra Molecular
AssayAssure® Platform and Product Pipeline

	Basic Chemistry			2nd Generation Chemistry		
Product Generation	1.0	1.1	1.2	2.0	2.1	2.2
Composition	Chaotrope + Chelator	Previous + Buffers		Previous + Purine or Pyrimidine		Previous + Proteinase Inhibitor*
Analytes	DNA/RNA & Small Molecules	DNA/RNA	Protein, hormones	Proteins, DNA, RNA	Cells	DNA, RNA, Cells, Proteins
Proposed Use	Preservation	Suppression of inhibitors of amplification technologies; Preservation				
Key IP and Status	▪ ***US No. 6,458,546 Issued 10/01/2002 (priority to 1997)*** ▪ US Pending filed 8/16/2001 ▪ US Pending filed 9/29/2008	▪ US Pending filed 9/12/2007 ▪ PCT Pending 9/12/2007	▪ US Pending filed 7/09/2007	▪ US Pending filed 7/09/2007 ▪ PCT Pending filed 9/12/2007	▪ US Pending filed 3/14/2008 ▪ PCT Pending filed 3/14/2008	▪ US Provisional Pending filed 7/03/2008

* Also includes Kosmotrope and/or Reducing Agent.
Source: Sierra Molecular; Health Advances interviews.

Appendix B

Sierra Molecular
AssayAssure® Applications By Market

Products	Clinical	Research	Environmental, Drugs of Abuse & Defense
Genelock® Urine Cup/Tubes – 15 ml tube, 4ml tube, 90 ml cup	CT/GC - Mol	Cancer Gene Transcripts - Mol (prostate and bladder cancer detection)	Performance Enhancing Substances
	Chem - Dipstick		
	Sediment - Instrument		
	Cells - Microbiology		
Genelock® Swab/Sponge Kit and Genelock Environmental®	CT/GC - Mol		Bird Flu - PCR
	Shigella - Mol/Micro	HIV - PCR	Environmental Pathogens - PCR
	Nasal Pharangeal Bordatella - PCR/Micro	Earth-Science Microbiology - PCR	Food Pathogens - PCR
	Herpes Simplex Virus - PCR		
Hemolock® Blood Tubes - 5 ml draw	Leukocytes - FC	Leukocytes - FC	
	Virus Detection - PCR/Array	Bacteria Detection - PCR/Array	
	Viral Load - PCR/Array	Virus Detection - PCR/Array	
	Viral Genotyping - PCR/Array	Viral Load - PCR/Array	
		Viral Genotyping - PCR/Array	
	CD4/CD8 - FC	RNA - Extraction Method Companion	
		Prokaryote & Eukaryote - Arrays	
Genelock® Bulk Chemistry – 230 ml bottle	STDs - Mol (for cups/tubes)	Prokaryote & Eukaryote - Arrays	
	Tissue Pathology - PCR	Earth-Science Microbiology - PCR	
Genelock Multiplex® PCR Applications (Mol Specimen Transport Tube)	Emerging STDs (Bacteria and Viruses) - PCR	Emerging STDs (Bacteria and Viruses) - PCR	

Product in Market / Ready for Market
Incremental Validation Required
Requires Clinical Trials and FDA Approval
New Product Line

Source: Sierra

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