University of Arkansas Microelectronics-Photonics Graduate Program
PhD Candidacy Exam – March 2007

Advanced Devices in Chemistry/Biology at the Micro to Nanoscale (including associated materials and processing)

PROBLEM TO BE SOLVED

Nitric oxide (NO) was regarded as a major component of air pollution until its discovery as a endothelium derived relaxing factor in 1987. Now we know that nitric oxide is produced by a variety of human tissues and is involved in the regulation of diverse physiological processes including neurotransmission, immure response and blood pressure regulation. Alterations in nitric oxide levels cause major diseases.

However, we will limit ourselves to nitric oxide levels in breathing air for this purpose. Nitric oxide is present in exhaled air of animals and humans in normal conditions. NO levels substantially increase in exhaled air in case of airway inflammation and is used to monitor inflammatory disease processes such as asthma. A normal NO concentration in expired air in humans is in the range 10–20 ppb in adults. In asthma patients, the exhaled NO values can reach concentrations well exceeding 100 ppb. Thus, measurement of exhaled nitric oxide is a simple method that may permit early detection of unsuspected lung diseases.

As a CTO of biomedical startup company Nitric Oxide - Detection Environment and Display (or NO-DEAD for the logo), you will be guiding a development of a device "BREATH NITRIC OXIDE TEST SYSTEM" to detect NO in expired breath of an asthma patient. Efforts should be focused on developing a non-invasive, simple and reproducible exhaled NO measurement technique. The two most popular current NO detection technologies use either chemiluminescence or electrochemical methods.

In chemiluminescence method, NO reacts with ozone (O_3) to generate excited nitrogen dioxide (NO_2^*) molecules. The NO_2^* molecule emits electromagnetic radiation (photons) during shift to lower energy state. In electrochemical method, NO is oxidized on the surface of electrode to form nitrosonium ion (NO^+) following an electron transfer. Thus, the current flow between a working electrode (on which NO is oxidized) and reference electrode is proportional to the amount of NO oxidized.

Your device should be one unit able to operate in stand alone mode and small enough to be handheld. The NO-DEAD target market will be either (1) one unit for each examination room in a first responder facility or (2) one unit per home with known lung disease patients.

In both of these cases it is important that the unit deliver an indication of the actual NO ppb concentration detected so the system may be used to determine changes in the patient health over weeks, but the system is not intended to be worn as a continuous monitoring system.

Because NO-DEAD has rights to significant intellectual property in the field of MEMS design and fabrication, the NO-DEAD CEO wishes you to provide a MEMS based solution to this problem to avoid potential licensing fees with other techniques. This requires that your proposed device should have at least one significant component that uses MEMS fabrication techniques. For example, this can be the reaction chamber (chemiluminescence method), electrode (electrochemical method) or some other component in some other detection mode that you propose for this system.

Some technical specifications that affect the NO-DEAD device:

1. Sample capture must be less than 30 seconds.
2. Display of results must be in less than five minutes.
3. Because of the shared usage of this sensor, no back-transfer of sampled air must ever be available to the next user.
4. A method for daily device calibration using commonly available materials and/or gases must be included.
5. Device size must be such that it can be held comfortably in one hand during use.

The device market is perceived to be mildly cost sensitive, but the marketing group needs your manufacturing cost evaluation of this MEMS based device for their initial market size analysis.

YOUR DELIVERABLE

Your task is to write an internal 15 page combined technology implementation and product realization plan for the NO-DEAD corporate officers describing your approach to the issues introduced above. In addition, be sure you also address at least all of the following:

Current Technologies - What is already being done in this area by other researchers, companies and governmental institutions? The current state-of-the-art for both the science and the implementation should be described, making use of diverse resources such as science literature, journals, conference proceedings, the internet, patents or other sources of existing public knowledge. Be sure to cite all references used.

Your design for Manufacturing – Device specifications have already been listed, as has the limitation that requires a MEMS based solution.

Manufacturing Flow - Detail the step-by-step procedure for producing the MEMS sensor within the device, as well as general information on the system manufacturing. Because the CEO is concerned with potential IP leakage if the device is built outside of the company, no subcontracting of the manufacturing or assembly of any proprietary component, or of the final device, outside of the company will be allowed.

Testing and Qualification - Describe a set of tests and demonstrations that you will use to demonstrate the effectiveness of your approach and to give confidence that the implementation of the solution will launch successfully. NO-DEAD cannot afford to lose market share, and needs to ensure that the all new product launches go smoothly.

Cost Analysis – Describe the elements of the cost analysis that would be performed before a final implementation decision could be made. You should include such things as the major cost items that would impact the implementation, which elements of your implementation solution would be handled in-house versus externally-sourced, major risk elements that could drive up costs if the primary path item fails, costs of IP licensing needed, etc. Be sure to include not just the "what", but also the justification and/or reasoning behind your decisions. Remember, the marketing team needs a good manufacturing cost estimate for the total system as the product reaches mature product stage in order to determine potential market size.

Intellectual Property - In an appendix to this exam, list in rank order of importance all IP sources that were consulted while formulating the answer, including the full list of examined documents along with key important reference data. For instance, if the IP source is a patent, include the patent number; title; inventor name; and assignee name. (The full list will not be counted as part of the 15-page limit.)

Within the 15 page proposal document you must fully discuss the three IP publications that are the most significant IP threats to your solution, making comparisons of strengths and weaknesses of these approaches relative to your own. Include your recommendations on how these IP threats should be handled.

Of course this is just a minimum list of issues you should consider. There may be many more, The point is that your report ***should contain the evidence*** needed to make an effective and compelling case to your CEO in order to insure that she makes the right decision.