APPENDIX

FORUM ON TUMOR MARKERS: QUESTIONS

A. GENERAL:

1. Tumor marker tests such as PAP and Bence Jones proteins have been around for a long time, so why the sudden interest among insurers and the need to hold a forum of tumor markers?

2. In her October 1991 article on tumor markers in the Annals of Internal Medicine, Dr. Susan Bates said, "Increasing our knowledge about the capabilities and limitations of existing markers will enable us to use them judiciously." Would everyone agree that this statement comes close to defining our mission for this two-day forum?

3. What does "new technology assessment" refer to and how does this relate to the forum and to today's session in particular?

4. What are our specific goals for this second day?

5. Should our discussion of tumor markers be limited to the life insurance side of our business, or should we also attempt to view this issue from the health side? Do we know the extent to which health insurers may be interested in this subject?

B. MEDICAL/SCIENTIFIC:

1. Is it correct to say that each tumor marker is unique and one should consequently be wary of blanket praise or condemnation?

2. What distinguishes that "general," i.e. "universal," marker from common markers such as CEA or PSA?

3. What are the various ways in which tumor marker tests can be used, and how are they actually being used by today's clinicians?

4. The majority of journal articles on tumor markers say that these tests are not yet suitable for population screening purposes. Is this true, and if so, why?

5. Is it possible to cite a fairly typical level of specificity and sensitivity for commonly used markers? Using a screening test with those properties and assuming a 1% prevalence of life-threatening cancer, what is the resultant "positive predictive value" of that scenario, and what does this mean?

6. Is it true that test kit instructions for many of these markers specify that the test be performed within 24 hours, and that until the test is run, the specimen be maintained at 4 degrees Centigrade? Why?

7. Is it true that diurnal variation of as much as 25% is not uncommon with some of the tumor markers?

8. Is it true that in the case of many tumor markers there can be significant differences in numerical results between various manufacturer kits; and therefore not only should the same kit be used when doing serial testing, but one needs to know which kits were used when comparing results from different sources?

9. Recently there has been a lot written about prostate specific antigen (PSA) and there is some confusion about what is now being recommended. Is Dr. William Catalona or any other recognized expert in this field now advocating that PSA be used as a stand-alone screening test?

10. Let's assume that life insurance companies begin using one or more tumor markers for screening purposes. Can we anticipate the general reaction of attending physicians upon hearing such news? What are likely to be their principal objections? Can we anticipate the reaction of organizations such as the American Cancer Society?

11. Back in 1988, when the Office of Technology Assessment (OTA) made their report to the U.S. Congress on Medical Testing And Health Insurance, they said that "tumor markers are limited in their applications" and "test manufacturers do not recommend tumor marker assays for screening use." Were these statements correct then; and, if so, have events of the last four years tended to make these statements obsolete?

12. How important is it that laboratory tests - especially those of a high profile nature - be understood and accepted by our nation's medical and scientific communities before they are installed into the insurer's underwriting process?

C. UNDERWRITING/ADMINISTRATIVE:

1. There are a number of potentially very attractive ways that tumor markers might be used to the benefit of
insurers and the clients they serve. What advantages does this technology offer to the insurance industry?

2. Can it be said that underwriters are threatened by five major medical entities (namely AIDS, alcohol abuse, CAD, cocaine [drug abuse], and cancer) and that the underwriter has relatively effective screening tests for the first four, but not the last? Is the fact that we have the HIV antibody test, liver enzymes, the ECG, the urine test for cocaine metabolites - but no test per se for cancer - the major rationale for development of usable tumor markers?

3. What are the most important considerations involved in the underwriters' selection of new biomedical tests?

4. Although we are not going to discuss any specific proprietary test, it deserves to be asked whether or not the use of any "proprietary" screening test creates problems for the insurer; and if so, what are those problems?

5. What are insurers likely to do in regard to prenotifying applicants that they may be subjected to tumor marker testing? Are special informed consent forms needed for tumor markers?

6. Adoption of special confidentiality protections for positive HIV antibody test results was demanded by advocates and policymakers, and such is already anticipated for genetic testing information. Why do these two classes of tests demand exceptional treatment; and do those same characteristics apply to abnormal tumor markers?

7. How are the insurance labs apt to notify insurers when tumor marker results are abnormal? How will insurers disclose abnormal results to the proposed insured? What sort of handling/disclosure problems can be anticipated, and do these suggest a preferable manner of handling abnormal results?

8. Does the fact that there are no clinical "gold-standards" for confirming or invalidating positive tumor markers create significant problems?

9. What are the down sides of the "false positive" tumor marker?

10. Insurers who raise cut-points (expand the normal range) to improve test specificity and lower "false positive" are, by definition, electing to ignore a certain percentage - perhaps a high percentage - of test results conventionally regarded as abnormal. Could doing so compromise that insurer's ability to later contest a cancer case involving material misrepresentation?

11. If an insurer initiates routine screening with one or more tumor markers, what risks are created by failing to notify the proposed insured when such test(s) are elevated?

12. If someone is tested by their doctor and told that they have some sort of abnormal tumor marker, are the questions traditionally included on "part two" of the insurance application sufficient to elicit an appropriate disclosure?

D. ACTUARIAL/FINANCIAL:

1. Based on both number and amount, how does cancer compare to other major causes of mortality?

2. Is the fact that mortality from cardiovascular disease has declined significantly since the 1960s, and the risk of cancer has correspondingly increased by virtue of these being competing risks, an important consideration in a discussion concerning the appropriate role of tumor markers in the underwriting process?

3. Five-part question:

   A) Can we estimate what percentage of applicants have cancer at the time they apply for insurance? By type of cancer? How does this vary by age? By sex?

   B) What proportion of these people have life-threatening cancer?

   C) Of those with a life-threatening cancer, what proportion are likely to actually die from their cancer?

   D) Of those applicants with a life-threatening cancer who are likely to actually die of that cancer, what proportion are - or could be - detected using existing underwriting screening methods?

   E) Of those with a cancer that will cause death and that cannot be detected by existing underwriting methods, what percentage can reasonably be expected to be detected by means of present day tumor markers?

4. How reasonable is it to suggest that the actuary has already priced for cancer and that there is really no need to fortify present cancer screening capabilities?

5. How likely is it that insurance rates can be lowered significantly if effective tumor marker screening practices are adopted?

6. Is it true that the moment a tumor marker becomes widely used by clinicians is the same moment that
insurers will have to seriously consider using the same test to defend against antiselection?

7. In the case of HIV, it is common to add the face amounts of declined seropositive cases and consider that sum to have been "saved." Why might this approach not be valid for business involving abnormal tumor markers? What does "length-time bias" mean and how might this affect protective value calculations?

E. MISCELLANEOUS:

1. One of the major reasons - if not the major reason - that tumor markers have not been used in medical practice is that these tests are too insensitive to detect significant numbers of people with early and, therefore, curable disease. Insurers might maintain that this need not be a key goal for the insurance industry and that the insurer's objective is simply to identify people with otherwise undetectable cancer, regardless of whether they have curable disease or not. Does this contrast pose a problem for insurers?

2. Are insurers driving the introduction of this technology?

3. Can medical directors, underwriters, actuaries and chief executive officers be stereotyped as to their probable initial reaction to this technology? How might those reactions vary and for what reasons?