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Faculty of Medicine
The University of
British Columbia

November 3, 2008

Dr. Gavin Stuart
Dean, Faculty of Medicine
University of British Columbia
Dean's Office - Faculty of Medicine
Woodward IRC Room 317
UBC Campus

Dear Dr. Stuart:

Re: Therapeutics Initiative Review

Thank you for giving us the opportunity to review the Therapeutics Initiative.

The review team consisted of Professor Jean Gray, Professor Emeritus, Departments of Medical Education, Medicine, and Pharmacology at Dalhousie University, Dr. David Henry, President and Chief Executive Officer of The Institute for Clinical Evaluative Sciences, and Dr. Lisa Dolovich, Scientist, Center for Evaluation of Medicines at St. Joseph's Health Care, and Research Director, Department of Family Medicine at McMaster University, Hamilton, Ontario, and chaired by myself in my capacity as Professor and Head of the Department of Orthopaedics, University of British Columbia.

The review took place on October 30th and 31st, 2008 in Vancouver. The review was initiated by you and notice of the review was disseminated widely throughout the University and beyond. Requests for submissions were sent and numerous admissions were received.

The review is based on a thorough evaluation of the program, which resides within the UBC Department of Anesthesiology, Pharmacology and Therapeutics. It involved reviewing numerous solicited and unsolicited submissions. In addition we reviewed some structured material that was provided to us by members of the Therapeutics Initiative as well as the UBC Department of Anesthesiology, Pharmacology and Therapeutics. These submissions and interviews are outlined in Appendix 1.

This report is structured as follows:

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⇒ ***Summary of the Therapeutics Initiative:*** The components of the TI will be discussed, and basic conclusions will be made based on our impression of the function of each program.
⇒ ***Detailed Narrative Review:*** A detailed review in response to specific terms of reference that were provided to us and are appended in Appendix 2.
⇒ ***Recommendations:*** A detailed set of recommendations regarding the TI will be provided.

Summary of the Therapeutics Initiative

The Therapeutics Initiative (TI) was established in 1994 as a body charged with performing critical assessments of available evidence regarding new and existing drugs, primarily to assist PharmaCare in provincial formulary decisions. TI was to provide academic drug assessments, independent from government, and as a part of the Faculty of Medicine at UBC. Over the years, the TI has assumed three primary roles:

⇒ Drug Assessment: The production of systematic reviews and evidence summaries on new and existing drugs, primarily for the use of the provincial government, but also for other agencies.
⇒ Pharmacoepidemiology: Post market surveillance of drugs – an academic activity that often leads to evaluation of various government and academic programs.
⇒ Education: The TI has established an excellent education program, geared primarily towards primary care physicians and pharmacists. A variety of educational tools are in use, such as
  - The Therapeutics Letter – a 2-page summary of recommendations regarding the use of medications. This is published every two months or so and is widely circulated to the medical and pharmacy communities in BC and beyond.
  - Annual Drug Review Course
  - The "Road-Show" – ad hoc educational events organized to meet local needs, primarily of family physicians.

Drug Assessment

Initially, the BC government, through contracts with TI that have been renewed over the years, funded TI to perform drug assessments. Subsequently, as the TI became a better-known national and international entity, work under contract to other bodies, such as the federal-provincial Common Drug Review and the Cochrane Collaboration, has been performed. For the most part, however, funding has remained primarily from the provincial government, giving rise to a perception of a conflict of interest and lack of transparency. Historically, the TI reviewed 30-40 medications per year with an annual budget of $1 million. Currently, about 20 drugs per year are assessed because the Pharmaceutical Services Division does not request reviews of drugs studied by the Common Drug Review. TI has performed assessments for the Common Drug Review, and while we heard criticism that the TI should not exist because of the recent establishment of the Common Drug Review (CDR), two facts became clear:

⇒ The CDR does not review all medications
⇒ For some of the drugs reviewed under the CDR process, the TI has provided the background assessments for the CDR.

Conclusion: There is a role for a formal academic structure in BC to perform independent structured assessments of new drugs.

Pharmacoepidemiology

The pharmacoepidemiology group is charged with post-market surveillance of drugs, and is equipped to be a strong academic unit. To date, the best academic productivity from the TI has been through this group. The work that this group performs is important from a research, educational and population health perspective. The work done by this group should continue.

Conclusion: There is a need for ongoing pharmacoepidemiology work that is a part of the UBC Faculty of Medicine and is not linked directly to government.

Education

The education arm of the TI has achieved international fame and has an excellent reputation. This committee received submissions (Appendix 1) from USA, France, Australia, New Zealand, Spain, etc... and from International Agencies representing individual members from very varied backgrounds vouching for the excellence that the TI brought to the area of unbiased drug education. BCMA representatives and family physicians also stated that this role is invaluable. On the other hand, the Pharmaceutical Task Force Report was critical of the TI providing education on drugs, and suggested that the Ministry of Health should provide such education. This committee concluded as follows:

Conclusion: There is a definite need for the educational program offered by the TI. This is best provided by UBC Faculty of Medicine and not by the Ministry of Health.

Detailed Narrative Review

This review team was established by the University of British Columbia Department of Anesthesiology, Pharmacology, and Therapeutics and provided with Terms of Reference outlined in Appendix 2.

Service Impact of the TI

The most striking finding of this review is the level of controversy that the Therapeutics Initiative has created within British Columbia. Overall, the opinions of the individuals interviewed, as well as those of the written submissions, have been very polarized. For example, the BCMA submission stated that the majority of the physicians in British Columbia are ambivalent about the Therapeutics Initiative. However, almost without exception, family physicians in British Columbia are supportive of the Therapeutics Initiative, particularly the educational arm. From the point of view of decision making in practice, family physicians appreciated the objective nature of the reviews published in the Therapeutics Letter. They also appreciated the continuing educational activities that the TI provided as an unbiased source of information to balance information received from industry-sponsored CME events. On the other hand, with a few exceptions, specialist physicians seemed to have the following concerns:

⇒ *Bias towards government and lack of independence*: there is a perception that the Therapeutics Initiative is biased towards government (that the mandate of TI is to cut costs), that the reviews are not all-inclusive, and that the summary of the findings is not always in keeping with the best available literature, or indeed specialty clinical judgment. These concerns had been voiced to the Head of the Department of Medicine at UBC, who commissioned a review of some of the findings of the TI by an independent expert in the field. The conclusions of this external review were that the TI review process followed best knowledge synthesis practice and that the findings were consistent with the best available evidence. These are very important findings as the Dept. of Medicine review was commissioned by a group of physicians who were opposed to the Therapeutics Initiative, and this speaks to the integrity of the TI assessments.

⇒ *The TI is responsible for limiting access to new drugs*: there is a misconception that the TI is responsible for recommending which drugs are covered. In fact, the mandate of the Therapeutics Initiative is <u>not</u> to provide recommendations but to provide a summary of the evidence. After examining a random selection of drug assessments, we found no evidence that the TI assessments actually make recommendations to the Pharmaceutical Services Division.

The methodology of TI assessments is too narrow: The specialists felt that the TI methodology, which is based on data from randomized controlled trials, is too restrictive, and other sources of information should be used. Based on expert opinion within this review committee, we felt that the methodology of TI is justified and is in keeping with national and international standards for the work of similar bodies elsewhere in Canada (eg Common Drug Review) and internationally. The review team agrees that non-randomized studies can be informative, particularly when investigating adverse drug effects, but most claims about efficacy are adjudicated on the basis of randomized trials. Expert opinion and advice on the interpretation of evidence is also important. A common complaint was that the TI did not consult adequately with experts when preparing evidence summaries, took little account of these views when they were offered, and provided no feedback to the experts. We found some substance for these complaints. The consultation process appears to have been limited and although the feedback was

included in the reviews that we scrutinized there was no evidence that it influenced the conclusions. We recognize that these reports are confidential and this limits the capacity of the TI to provide feedback to informants. However integrating evidence and expert opinion is a difficult process and is not usually required of groups charged with providing evidence summaries. The review team considers that the responsibility for obtaining expert opinion and interpretation of evidence summaries should fall on the Ministry, not the TI.

Conclusion: The process by which the TI assesses drugs meets the standards of scientific quality and no evidence of bias is present in these reports, based on this committee's review of a randomly selected sample of assessments. TI reports use methodology that is applied and accepted worldwide. Expert Opinion is an important component of the process but consultation should be the responsibility of the Pharmaceutical Services Division not the Therapeutics Initiative.

The Academic Role of the TI within the UBC Faculty of Medicine

As an academic institution, the TI is charged with academic excellence in terms of research and teaching. Traditionally, academic productivity is measured by peer reviewed grants and peer reviewed publications. Clearly, the numbers of peer reviewed publications from TI and the numbers of peer reviewed grants to TI have been modest. Lately, however, with the maturation of TI, and with recruitment of new investigators, particularly in pharmacoepidemiology, original research and the publication record has improved. This committee tried to probe for reasons for the modest academic output.

- *The confidential nature of material reviewed:* It became clear that while the meta-analyses and systematic reviews of the TI meet international standards for excellence, PharmaCare and the Pharmaceutical Services Division provide the materials to be assessed to TI. That material has been submitted to those entities by industry *in confidence*. For this reason, any assessments resulting from that material would not be publishable in peer review journals, and certainly could not be made public on the TI website to interested stakeholders such as physician and patient groups, because the source material was marked as *commercial in confidence* by the pharmaceutical industry. This is a dilemma that faces not only the TI but also other similar bodies elsewhere in the world. When compiling a submission even information that is already in the public domain may be rendered confidential when it is included in a body as part of a pharmaceutical company therapeutic claim. In our interview with representatives of the pharmaceutical industry, this topic was raised but not resolved. This confidentiality issue has not only led to a low number of publications by TI in the peer reviewed literature, but has also led to criticism of TI by the pharmaceutical industry as well as some specialist physicians and directors of research institutes, concerning *the lack of transparency in the deliberations of the Therapeutics Initiative.*

Conclusions: 1. The issue of transparency needs to be resolved. 2. Drug assessments should be submitted to peer-reviewed journals and/or made public. The confidentiality issue should be addressed by the Ministry of Health to assure public transparency of the assessments.

- *Collaboration with others:* There is little collaboration between the TI and similar bodies within the University and elsewhere. Several bodies within the University of British Columbia are performing complementary and potentially synergistic work, such as the Center for Clinical Evaluation and Epidemiology (C2E2) at Vancouver General Hospital, the Centre for Health Evaluation and Outcome Sciences (CHEOS) at Providence Healthcare, the Center for Health Services and Policy Research (CHSPR) at the University of British Columbia, and the Child and Family Research Institute at BC Childrens' Hospital. Members of the TI, as it exists at the present time, could collaborate with these groups to pursue peer reviewed funding for their academic activities and to participate in original research.

Conclusions: TI should increase collaboration with similar existing units at UBC and elsewhere. Through collaboration, TI could pursue peer-reviewed competitive funding and increase the number of peer-reviewed publications.

- *Education:* Our review of the educational arm of the TI has been very positive. This is well received by the recipients of this educational effort. The educational component is in keeping with the academic mandate of TI within the University. We were particularly impressed by the variety of educational techniques used such as podcasts, the Road Shows, the annual Drug Course, and the Therapeutics Letter. Many of the TI publications, though not considered as peer-reviewed publications, are in keeping with the educational mandate of the university. Based on our review, we found there is a definite need for such educational activities and such educational activities need to be maintained. However, we noted that there is less effort being made to develop novel educational techniques and to study outcomes of current educational techniques. There is an opportunity within the educational arm of the Therapeutics Initiative to collaborate with other educational centers within the University, such as the Center for Health Education and Scholarship (CHES), to enhance the scholarship associated with this impressive educational outreach.

Conclusions: The educational mandate of TI needs to be maintained and strengthened. Novel educational methods should be developed and evaluated. Collaboration with educational centers as CHES should be encouraged.

Public perceptions of TI:

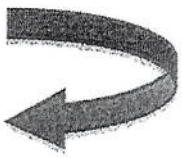
Despite the positive reviews in the above areas, we noted some areas of potential improvement.

Transparency: Concerns were raised that the full assessment reports of the TI are not made public and that the stakeholders are not kept informed of the TI's conclusions. Additionally, there is a misconception that TI makes drug approval recommendations to the Ministry. The confidential nature of submissions by the pharmaceutical industry to the Pharmaceutical Services Division makes public disclosure difficult, and is a major barrier to transparency. Earlier sections of this report outlined the issues related to confidentiality and transparency. The current drug assessment process includes:

- A submission from the pharmaceutical industry to Pharmaceutical Services Division which commissions TI to perform an assessment.
- The TI seeks extra input from clinical experts and summarizes the comments of the clinical experts in its assessment.
- The assessment is submitted back to the Pharmaceutical Services Division which considers the assessment, amongst other evidence, at the Drug Review Committee, and a recommendation is made regarding the listing of drugs.

At present, members of TI are invited to be present at the Drug Review Committee meetings. One member of TI has had voting rights at both the TI Scientific Investigation and Education Committee and the Drug Review Committee, in the past. This has led to problems in terms of transparency.

Conclusions: A different structure for drug assessments is recommended and should include the following processes:



- An academic body within the University of British Columbia, not funded directly by government, should provide an independent assessment of drugs based on information provided from the pharmaceutical industry to the Ministry, as well as other relevant, if present, randomized controlled trials.
- The methodology should continue to be primarily review of randomized controlled trials.
- Novel techniques that could incorporate other evidence should be developed and evaluated. Once these techniques are proven, they may be incorporated within the assessment process but should not be incorporated until critically studied, reviewed, and submitted to the peer review process.
- The academic assessment body should not obtain external reviews from clinical experts. Instead, the academic assessment should summarize the available evidence and send it back to the Pharmaceutical Services Division. The Pharmaceutical Services Division then should seek input from a committee of clinical experts.
- The panel of experts should be chosen based on their clinical expertise. The University of British Columbia, the Faculty of Medicine, and possibly the BCMA,

could provide names of such experts to the Ministry of Health Services. A minimum of three clinical experts should review the reports.

- Industry should review the assessment reports for factual errors and to ensure that confidential information is not included in the public disclosure of such reports.
- These reports should enter the public domain and be published on the website of this new entity as well as that of the Ministry of Health Services and anywhere else that is deemed appropriate. Simultaneously, these reports can be reformatted in a manner that is compatible with publication in the peer reviewed literature and, if appropriate, could be submitted for publication.

By following such process, full transparency will be achieved. The final decision of the Drug Review Committee will be based on the drug assessment report, and on feedback from clinical experts. Any perception that the TI or whatever structure replaces it, is responsible for listing or lack of listing of medications will be removed. Furthermore, there should be no voting members on the Drug Review Committee who have been involved in the drug assessment process or in giving feedback to the Pharmaceutical Services Division during the drug review process. Such experts may be invited to answer any questions from the Drug Review Committee, but should be dismissed during the Committee's deliberations and voting.

It is also clear that within British Columbia there is resistance to the name *Therapeutics Initiative*. However, the name *Therapeutics Initiative*, as a brand, has a favorable international reputation. While it is not the mandate of this review team to determine what happens to the name *Therapeutics Initiative*, it must be made clear to the TI opponents that the title *Therapeutics Initiative* has an excellent international reputation.

Recommendations

1. The current Therapeutics Initiative has experienced misinterpretation and misunderstanding. For this reason, the current structure of the Therapeutics Initiative cannot continue. Nevertheless, there is a need for an academic institution to serve as a resource of therapeutic knowledge, to provide objective assessments of evidence about new drugs, and to offer unbiased education in therapeutics.

RECOMMENDATION #1: The current Therapeutics Initiative Program should be replaced with a different structure

2. The current structure of the Department of Anesthesiology, Pharmacology and Therapeutics consists of a Section of Anesthesiology, and a Section of Pharmacology and Therapeutics. The clinical activities of the members within the Therapeutics Initiative are very distinct from other members within the section of Pharmacology and Therapeutics. In particular, the academic work of the members of the Therapeutics Initiative is more within the realm of epidemiological evaluations, systematic reviews and meta-analysis. Furthermore, the graduate students have little in common with the graduate students in pharmacology, which is centered on basic science research. For this reason, the Department of Anesthesiology, Pharmacology and Therapeutics should be reorganized into three sections. These would be (in alphabetical order):

   - The Section of Anesthesiology
   - The Section of Pharmacology
   - The Section of Therapeutics

   A Section Head for the new section of Therapeutics should be appointed by the Head of the Department of Anesthesiology, Pharmacology and Therapeutics. The process of appointing such a head can be at the discretion of the Department Head, but the new Section Head should not be the Head of the *Therapeutics Initiative* or the structure that replaces TI, and there should be a fixed term for the appointment, with a review at the end of the term. The term can be renewed once at the discretion of the Department Head, with the approval of the Dean.

RECOMMENDATION # 2: The Therapeutics Initiative should be replaced with a new ***Section of Therapeutics*** within the Department of Anesthesiology, Pharmacology and Therapeutics

3. For the section of Therapeutics to be functional and to be academically productive, stable funding must be ensured. There will be a role for the Section of Therapeutics in providing assessments of drugs, a process of benefit for the people of British Columbia. For this reason, the section should be appropriately funded by the University of British Columbia, Faculty of Medicine. This review team is aware of the lack of funds within the Faculty of Medicine to establish a new well-funded program. For this reason, the Government of British Columbia should provide adequate funding

to the Faculty of Medicine to establish the Section of Therapeutics. The current funding of the Therapeutics Initiative at $1 million per year is not sufficient to maintain academic productivity and provide high quality drug assessments in a timely manner. Based on international benchmarks, the Province of British Columbia is receiving excellent value for the funds provided to TI for drug assessments. In order to allow faculty members within the new Section of Therapeutics to be academically productive, there needs to be:

- Adequate funding of the faculty within the Section of Therapeutics to avoid reliance on the "grant tenure" track and to permit the establishment of three additional and permanent F-slots within the section, to complement the existing F-slot held by Dr. James Wright. This would facilitate the establishment of leadership for three areas within the Section. These areas would form three semi-autonomous but inter-related centres:

A. The Centre for Drug Evaluation:

This centre's mandate would be to develop and evaluate novel techniques in the assessment and synthesis of information concerning drug efficacy and safety. It would also be charged with providing drug assessments to the Pharmaceutical Services Division of the Ministry of Health. Any contractual arrangement for such work should be between the Government of British Columbia and the UBC Faculty of Medicine and not with the Department of Anesthesiology, Pharmacology and Therapeutics or any of its sections. This would remove any perception of government bias in the assessments and would allow for more transparency and accountability. Drug assessments would be submitted to the Pharmaceutical Services Division which would then seek external consultation as has already been mentioned earlier in this report. Once these assessments have been studied by the designated Ministry of Health expert reviewers for comment and by industry for correction of factual errors, the reports could then be reformatted and submitted for publication in a peer-reviewed journal. The full reports would be made publicly available to stakeholders, including physician groups, patient groups, and industry. This would address the issue of transparency.

B. The Centre for Pharmacoepidemiology:

The main mandate of the Pharmacoepidemiology group would be post-marketing surveillance of medications. This Centre would have a strong academic component. This group should collaborate with similar groups elsewhere within the University, as has already been discussed earlier in this report.

C. The Centre for Education in Therapeutics

The third group within this section would be mandated with education. There is already a strong educational arm within the Therapeutics Initiative and the activities should continue and be enhanced within the educational

area of the Section of Therapeutics in collaboration with existing education centers such as CHES. The current educational initiatives of the Therapeutics Initiative would be folded within this section, and publications such as the Therapeutics Letter should continue and be enhanced. Because of the substantial unfunded service component for this section, a sufficiently large Faculty of Medicine endowment should be established to fund the educational activities of this Centre. In addition to continuing medical education, this Centre will also be responsible for teaching medical students, residents, and pharmacy students the science of therapeutics. The establishment of a Royal College accredited residency program in Clinical Pharmacology, which would be the only such program west of Ontario, should be considered.

Each centre would be accountable to the Section Head and through him/her to the Department Head and subsequently to the Dean.

Funding for the educational arm and funding for the drug assessments should be completely separate in order to avoid any perception of bias. An endowment, as already discussed, should be established for the educational component. In addition, a funding arrangement between the Faculty of Medicine and the Government of British Columbia for four F slots including the one existing at the present time should be established.

RECOMMENDATION # 3: Stable arms-length funding for the Section of Therapeutics is necessary.

4. Because of the public service component of the Section of Therapeutics, there has to be recognition of all stakeholders, including the University, the Department of Anesthesiology, Pharmacology and Therapeutics, the Ministry of Health Services, the pharmaceutical industry, physicians and physician groups, as well as the public and patient advocacy groups. For this reason, the Section of Therapeutics needs a governance structure that fosters stakeholder input. An Advisory Board with wide representation is recommended. The Advisory Board would provide advice in areas such as strategic direction, policy development, and similar high-level activities. Representation and input from the following groups would be valuable:

   - Faculty of Medicine Leadership
   - Clinical Departments within the Faculty of Medicine
   - The BC pharmaceutical industrial sector
   - BC Medical Association
   - Faculty of Pharmaceutical Sciences
   - Clinical Pharmacy within the Community
   - Patient Groups
   - Community Businesses
   - Head of the Department of Anesthesiology, Pharmacology and Therapeutics
   - Other members at the discretion of the Head of the Department of Anesthesiology, Pharmacology and Therapeutics and the Dean of Medicine.

A Director to manage the finances, the website, and education material required or created by the Section must be hired.

RECOMMENDATION # 4: An enhanced Administrative Structure for the Section of Therapeutics with transparency and accountability is required.

5. Collaboration between the Section of Therapeutics and local research centers with related activities such as the Center for Clinical Epidemiology and Evaluation, Centre for Health Evaluation and Outcomes Sciences (CHEOS) at Providence Healthcare, the Child and Family Research Institute, the Vancouver Coastal Health Research Institute, the School of Population and Public Health, and the Centre for Health Sciences Policy Research (CHSPR) is recommended. Links with the Faculty of Pharmaceutical Sciences should be established. The lack of dialogue between this review team and the Faculty of Pharmaceutical Sciences was obvious and further collaboration would improve the academic output of both groups interested in drug therapy.

RECOMMENDATION # 5: The Section of Therapeutics needs to establish collaboration with similar academic units at UBC and elsewhere.

6. The service component of the Section of Therapeutics, in particular its drug evaluation arm, should be limited to a set yearly maximum number of drug assessments in order to give ample time for independent academic activities.

RECOMMENDATION # 6: There needs to be a balance between the service component of the Section of Therapeutics and its commitment to academic contributions.

7. The Section of Therapeutics should be encouraged to seek external sources of funding such as peer reviewed grants in addition to the contract work with external agencies currently being undertaken.

RECOMMENDATION #7: There is a need for the Section of Therapeutics to pursue external peer-reviewed funding.

8. No member from the Centre for Drug Evaluation or any other member within the leadership of the Section of Therapeutics should have voting rights on any committee that makes decisions regarding listing of drugs within British Columbia.

RECOMMENDATION # 8: There needs to be transparency when dealing with government policy decisions.

9. A concern was raised regarding the methodology of drug assessments within British Columbia. This committee disagrees with this request as the process used for drug assessments by TI is the national and international standard. However, the Section of Therapeutics should consider a new research program of enhanced review methodologies that might become an academic focus of the section, particularly for the Centre for Drug Evaluation. With time, as novel methodologies become available, they may be incorporated into the drug review processes but only after their validity and reliability has been documented.

RECOMMENDATION # 9: There needs to be an academic focus on drug assessment methodology

10. We recommend that an effective communication strategy be established by the Section of Therapeutics in order to avoid the misconceptions that have plagued the Therapeutics Initiative. The Faculty of Medicine as well as the various Health Authorities within the region have access to excellent communication departments and collaboration with such departments should take place. There has to be better communication with various stake holders, including industry, in order to maintain a transparent and open drug assessment and educational process.

RECOMMENDATION # 10: There needs to be an enhanced communication strategy

Review of the Pharmaceutical Task Force Report

11. Review of the Pharmaceutical Task Force Report (PTFR): The report of the Pharmaceutical Taskforce to the Honorable George Abbott, Minister of Health, Province of British Columbia, dated April 2008.

    The committee felt that this report was lacking in substantive evidence. The report has twelve recommendations, and two of these recommendations are relevant to the TI.

    Recommendation 4 was: *"The Ministry of Health should establish a New Drug Review Resource Committee to carry out the drug submission review role currently performed by the Therapeutics Initiative. This new DRRC should also provide for a registry of experts that will substantially widen the array of expertise available to offer advice and recommendations of the therapeutic value and cost effectiveness of new drug therapies."*

    Recommendation 12 related to replacing or reconstituting the Therapeutics Initiative and read: *Subject to recommendation 4, if the Therapeutics Initiative is maintained; actions must be taken in the following areas:*

- *The governance, membership and accountability standards associated with the operation of the Therapeutics Initiative will require substantial improvement*
- *Steps must also be taken to renew and revitalize the panel of experts the Therapeutics Initiative relies upon to discharge its obligations:*
- *The function of the Therapeutics Initiative should be focused on therapeutic evaluation. Activities beyond that core mandate such as public education should be reassigned to the PSD's Drug Utilization Unit where an accountable process can be implemented to assure unbiased and evidence based practices:*
- *The practice of having members of the Therapeutic Initiative also participating in the work of the Drug Benefits Committee should be terminated.*

One of the mandates of this review team is to comment on the recommendations of the Pharmaceutical Taskforce Report (PTFR), with reference to the Therapeutics Initiative.

Comments on the PTFR recommendation # 4: We partially **agree** with recommendation 4 that a different mechanism for drug reviews be established. However, we **disagree** that there should be a role for the Ministry of Health Services in education. Our recommendation is:

RECOMMENDATION # 11: The Section of Therapeutics should provide independent assessments of drugs, at the request of the Ministry as well as others. The Ministry of Health Services should request a panel of experts, chosen in collaboration with the Faculty of Medicine and the BCMA, to review the assessments. We also feel that industry should have the opportunity to review the assessments for factual errors prior to the reports being forwarded to the Drug Review Committee.

Comments on the PTFR recommendation # 12: We **agree** that the governance and accountability standards associated with the operation of the Therapeutics Initiative (which we have recommended be replaced with a Section of Therapeutics) will require improvement, and we have offered some recommendations for such an improvement. We also partially agree that the panel of experts of the Therapeutics Initiative relies upon to discharge its obligations be renewed. This will be done through the panel of clinical experts outlined above. However, a core number of individuals with the necessary skills in drug assessment need to be maintained in order to provide quality assessments as well as academic productivity and this would be a major function of the Section of Therapeutics.

We **disagree** with the recommendations that education regarding drugs and therapeutics in British Columbia should be within the control of the Ministry of Health Services. This is an academic activity and must continue within the Section of Therapeutics at the University of British Columbia. It needs to be stressed that the Therapeutics Initiative brand is extremely well known internationally and great care has to be taken not to destroy this excellent reputation.

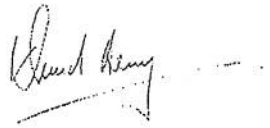
Finally, *we **agree** that members of a drug assessment team not participate as voting members in any decisions that determine whether drugs are to be listed or not on the provincial formulary. Clearly, such committees may have questions for the assessors and the assessors may be consulted to explain the findings of their work but should not participate in voting activities.*

Respectfully submitted

Bassam A. Masri, MD, FRCSC

Jean Gray, CM, MD, FRCPC, FCAHS, LLD (Hon), DSc (Hon), FRCP (London)

Lisa Dolovich, BSc, MSc, PharmD



David Henry, MD, MRCP, FRCP (Edin)

Submissions to the Review Committee:

1. A letter from the BC Provincial Blood Coordinating Office, a program of the Provincial Health Services Authority.

2. Several submissions from specialist physicians and specialist associations from within British Columbia, all of which except one were critical of the T.I.

3. A submission from a Professor of Medicine in Baltimore, Maryland who was extremely supportive of the Therapeutics Initiative and felt that the educational role of the TI has been exemplary.

4. A letter from a Professor at the University of Montréal. This letter was very supportive of the TI.

5. A letter from a resident in anesthesiology who commented positively about the influence of the TI on his education.

6. A letter from a Clinical Instructor at the Harvard Medical School who was supportive of the Therapeutics Initiative as an unbiased source of information on therapeutics.

7. Two letters from WorkSafe BC supportive of the TI.

8. Submissions from all over the western world, including Australia, Canada, USA, France, Germany, Italy, The Netherlands, New Zealand, Portugal, Spain, and the United Kingdom strongly supporting the Therapeutics Initiative as one of the best sources of information and education about pharmaceuticals in the world.

9. A letter from a group of rheumatologists and from the leadership of the Mary Pack Arthritis Program. This was critical of Pharmacare (and indirectly TI) for not releasing biologics in a short period of time.

10. A letter from a private citizen in British Columbia who is highly supportive of the TI. This letter quoted how the TI has been able to perform regression analyses of the benefits of new drugs and has helped the Pharmaceutical Services Division curtail the rapid escalation of drug prices. It also stated that the TI should enhance its research capabilities in the pharmacoeconomic arena, and also commented that the TI allow other jurisdictions to assess innovation. The committee did not agree that the TI should move in this direction.

11. Several submissions from family physicians from all over BC. These were supportive of the TI.

12. A letter that was critical of the academic output of the TI.

13. A peer-reviewed academic publication that showed that evidence based drug coverage policies in British Columbia had no statistically significant negative effects on recent BC based pharmaceutical research and development.

14. In addition to the written submissions, we had two days of interviews with a variety of individuals. The opinions expressed to us by the individuals interviewed were very insightful and formed, in part, the basis for our recommendations.

15. We reviewed the Pharmaceutical Task Force Report (2008):

16. We obtained three randomly selected reviews from the Therapeutics Initiative drug reviews. We reviewed the reports for content and accuracy and found that the reports were free of bias, and all the relevant material that should have been included was indeed included. We also noted that the opinions of expert clinical reviewers were actually appended to the end of report, prior to submission.

17. We reviewed:

    - the last two Annual reports of the Therapeutics Initiative.

    - a submission from the Better PharmaCare Coalition, dated October 2008.

    - a document that outlined the structure, policy and procedures of the Therapeutics Initiative.

    - the reports from the Auditor General of British Columbia on managing the cost of drug therapies and fostering appropriate drug use and reports on managing PharmaCare. These were supportive of the role of TI in controlling drug cost through unbiased reviews of drugs.

Appendix 2

Terms of Reference: Therapeutics Initiative External Review

The External Review of the Therapeutics Initiative (TI) has been organized to review the academic value of the TI, its management structure, its leadership and its funding.

1. The reviewers are asked to consider the following:

   a. Does the quality of the research done by the TI meet international standards for excellence?
   b. Is the publication record of the TI and the site of publications indicative of a high degree of academic success?
   c. Do the processes by which the TI reviews medications meet the highest standards of scientific quality? Is there any evidence of a bias in these reports?
   d. Does the management structure of the TI provide the appropriate support for its activities and are the components of the TI independent enough of each other to provide unbiased reporting.
   e. Are there opportunities for the TI to achieve peer-reviewed funding for a part of its activity?
   f. Is the current funding model open to abuse and, if so, how can it be modified to assure freedom from conflict of interest (real or perceived)?
   g. Does the recent "Task Force" report fairly express a need for a radical change in the TI?
   h. Would "contractual funding" (i.e.: the MOH pays for specific projects by the TI instead of providing global funding) improve the perception of bias or make it worse?
   i. Is the leadership of the TI effective both in leading the scientific mandate of the TI and making its findings available to health care providers and the public? Are there ways that public perceptions and health care profession perceptions can be improved?

2. The reviewers will report directly to Dr. Brian Warriner, Head of the Department of Anesthesiology, Pharmacology and Therapeutics who will share the report with the Dean of the UBC Faculty of Medicine.

3. The reviewers should feel free to comment, as appropriate, on the recommendations of the "Task Force".

4. The reviewers will receive a package of information, including the "Task Force" report in advance of the review and a final package a week before the review.

5. The reviewers should consider both the verbal information received during interviews and the written information provided in making their