Review of DST/NRF Centre of Excellence for Biomedical TB Research (CBTBR)

Dates of Review
12 and 14 March 2009

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Executive Summary
A review of the DST/NRF Centre of Excellence (CoE) for Biomedical TB Research was held on March 12th-14th 2009. The review covered the activities of the CoE for the five years from its inception in Sept. 2004 to 2009. The review panel consisted of three members, two from the USA and one from S. Africa. Extensive documentation was provided prior to the review that consisted of a full-day of briefings, meetings and interviews at each of the 2 sites of this bi-nodal CoE. This CoE brings together TB research groups with top world-wide reputations at the Univ. of Witwatersrand and National Health Service Laboratories (NHLS) in Johannesburg headed by Dr. Valerie Mizrahi and at the Stellenbosch University in Cape Town by Dr. Paul van Helden.

This unique bi-nodal CoE has made extraordinary progress during the last five years in research productivity (over 112 publications), establishing itself as the true center for basic and translational TB research in S. Africa, training and supervision of MSc and PhD students, expansion of international collaborations and funding, establishing and maintaining new networks and providing service. DST/NRF funding for this CoE has been an essential source of core funding that has allowed the CoE to develop, grow and leverage the CoE funding for extensive internationally-collaborative and recognized cutting-edge TB research in S. Africa.

At this critical 5-year junction of the highly innovative and successful CoE program of the DST/NRF, this CoE is poised to continue exceeding the requirements of the program and expand the scope and impact of TB research and training in S. Africa to help combat the enormous TB pandemic that is ravaging the country. This Co-E with adequate long-term support will be instrumental in delivering better approaches to the prevention, diagnosis and treatment of TB by its unique position in the world as a top TB research center in the middle of a TB endemic setting.

The panel has the following key recommendations that are outlined below and discussed in more detail in the body of the document that will allow the CoE to meet its promise.

Key Recommendations
1. Increase capacity for TB research throughout S. Africa by investing in collaborative projects between the CoE and institutions willing to expand TB research:
   Specifically, there is an urgent need to integrate the planned massive expansion by the Howard Hughes Medical Institute (HHMI; USA) at KwaZulu Natal University (KZN) in TB research with the goals and objectives of CoE to enhance access to technology, for career development for CoE trainees and transfer of CoE expertise for the success of the HHMI enterprise.

2. Increase capacity for TB research throughout S. Africa by forming consortia to acquire key technology and expertise:
   Specifically, the development of bio-informatics and/or proteomics platforms either at the CoE sites or between the CoE unit at Stellenbosch and other academic institutions in South Africa such as the University of the Western Cape (UWC).
3. **Urgent need to clarify the long-term financial commitment from DST/NRF beyond the current 10 year commitment to the CoE program:**
   Specifically, this CoE is currently in year 6 of 10 and lack of long-term commitment will limit the ability to commit to MSc and PhD training beyond year 7.

4. **Increased funding for this bi-nodal CoE, the CBTBR, for years 6-10:**
   Specifically, given the demonstrated excellence and success of this CoE in exceeding the DST/NRF’s criteria for success with a very limited budget that has been used and administered judiciously, increased investment in the CBTBR will allow immediate expansion of research scope, training and outreach.

5. **Opportunity to strengthen the interactions between the two nodes of this CoE:**
   Specifically, developing collaborative joint projects, offering student rotations between sites, having joint video-conferences to enhance exchange of research ideas, technologies and identification of new research opportunities.

6. **Creation of career paths for early and midlevel faculty in biomedical research:**
   Specifically, the creation or existence of posts for biomedical research within universities or research institutions appears to be extremely limited; this greatly impairs the ability of S. Africa to retain highly trained and internationally competitive research scientists, risking their departure abroad and loss to the S. African biomedical research enterprise.

7. **Career counseling for non-academic career paths:**
   Specifically, the relative isolation of the two nodes of the CoE from their parent institutions limits the exposure and knowledge of MSc and PhD students about careers in biomedical science beyond the immediate focus of their research and the academic career path.

8. **Continued appropriate recruitment of black African students to the CoE:**
   Specifically, there needs to be recognition on the part of DST/NRF that the critical shortage of Black African students pursuing higher education in the biomedical sciences will continue to hamper this CoE’s ability to recruit black African students.

9. **Relieve the administrative burden placed on the CoE by the NRF:**
   Specifically, the requirement for separate annual reports and business plans, monthly budgetary/fiscal reports, periodic self-assessments and strategic plans burden CoE staff and principals unnecessarily, and take resources and time away from research and training.
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**Background**

The Department of Science and Technology (DST) through the National Research Foundation (NRF) developed a framework for the creation of “NRF Centres of Excellence” (CoE) in 2003. Seven physical or virtual centers have been created to concentrate existing research capacity and resources to foster long-term collaboration across disciplines thereby enhancing research experience and capacity development. CoE’s are sponsored by DST and administered by NRF.

The Centre of Excellence for Biomedical TB Research (CBTBR) was established in September 2004 and is a bi-nodal Centre of Excellence (CoE) that is hosted jointly by Stellenbosch University (SU) and the University of the Witwatersrand (WITS). The CBTBR is the only DST/NRF CoE that is hosted jointly by two institutions. The creation of the CBTBR brought together two well-established tuberculosis (TB) research groups with long histories of support by the Medical Research Council (MRC) and the NHLS, which previously had very little formal contact, namely the MRC/SU Centre for Molecular and Cellular Biology (CMCB) directed by Prof. Paul van Helden and the MRC/NHLS/WITS Molecular Mycobacteriology Research Unit (MMRU) directed by Prof. Valerie Mizrahi.

The mandate of the CBTBR is to research new tools for the diagnosis, treatment and prevention of TB. *Mycobacterium tuberculosis*, the causative agent of TB, is estimated to infect one third of the world’s population and is responsible for the largest number of deaths attributable to a single infectious agent. Based on the indicators contained in the WHO 2008 Report on global TB control released in March 2008, South Africa rose from a ranking of seventh to fourth in the world in terms of the number of incident cases of all forms of TB in 2006. The urgency of the need for new and improved tools for the diagnosis, treatment and prevention of TB simply remains self-evident. Experimental approaches that are based on a post-genomic research strategy have a particularly important role to play in this regard.

The strategic objectives of the CBTBR were to make significant contributions to the development and evaluation of new tools for controlling TB and to human resource development aimed at creating significant capacity in this important area of biomedical research through research in three thematic areas: (I) target validation and characterization through basic research in mycobacterial metabolism; (II) bridging the gap between basic and clinical TB research; and (III) host responses to TB.

The research plan of the CBTBR is placed in the context of a wide network of regional, local and international collaborations and linkages and uses the combined knowledge and expertise at both nodes as a platform for brokering information and rendering relevant services at various levels.

*Paraphrased and edited from text provided by NRF and CBTBR*
Purpose of Review

1. Review past performance of the CoE *vis a vis* the Key Performance Areas (KPA) from Sept. ’04 through 2008.
2. Identify past and future risks and threats to continued growth and performance of this CoE from Sept. ’04 through 2013.
3. Assess the institutional support for the CoE by its constituent Universities, NHLS, MRC, NRF, and DST.
4. Assess opportunities for the CoE in the setting of the current national and international funding climate for TB research.

Review Methodology

A review of the DST/NRF Centre of Excellence (CoE) for Biomedical TB Research was held on March 12th -14th 2009. The review covered the activities of the CoE for the five years from its inception in Sept. 2004 through 2008. The review panel consisted of three members**, two from the USA and one from S. Africa as listed on the front page. Extensive documentation was provided prior to the review.

The panel was briefed by Dr. Andrew Kaniki of NRF on the purpose and scope of the review and the responsibilities of the panel in terms of reporting before its review of the node at the University of the Witwatersrand. Each node was visited and reviewed for a full day that consisted of briefings, meetings and interviews at each of the 2 sites of this bi-nodal CoE with senior faculty, students and staff.

**It should be noted as part of full disclosure that Dr. Murray has collaborative research projects with investigators at both nodes and Dr. Boom collaborates with Dr. Walz at Stellenbosch; neither Drs. Murray and Boom receive funding from the CoE.
Key Performance Areas

Research

Strengths: Scientific progress, productivity and expanding scope of research have been outstanding during the last 5 years. This is reflected in an excellent publication record that far exceeds the requirements set out by DST/NRF. As shown in Appendixes I and II, there is a broad distribution of senior and junior authors, students as co-authors, publication in excellent journals with high impact factors, and co-authorship with major international collaborators. In addition, the groups have produced numerous book chapters, invited reviews, technical reports and patents. The outstanding research productivity and reputation of the CoE has resulted in attracting and retaining outstanding MSc and PhD students (see below for more details), as well as extensive international collaboration and funding. The laboratory infrastructure has been markedly improved and strengthened over the last 5 years. There is a strong research ethos in both nodes of the CoE reflected in an informal environment for students, senior and junior investigators to interact, ready accessibility of principal investigators (PI’s) and faculty, the fact that the PIs work in the labs and a strong collaborative team spirit. Thus the resources provided by NRF to the CoE have been very effectively leveraged for a remarkable expansion and scope of research productivity, training and collaboration.

Weaknesses: There are no weaknesses. The CoE has exceeded all research requirements set by DST/NRF. Whereas development of collaborative research projects between the two nodes, despite very effective and close leadership by Drs. Van Helden and Mizrahi, has been slow, there now are a number of potential projects being considered for true collaborative research between the two nodes in the next year.

Opportunities: These two research teams are optimally poised to expand the scope of their TB research because of their unique situation as a top basic and translational TB research groups located in one of the worlds highest burden TB setting. They will be able to be equal partners or leaders in the increasing number of international collaborative networks of TB research that are developing driven by external funders such as the Gates Foundation, NIH, Welcome Trust, European Community, etc. The evolution of the TB epidemic in S. Africa will continue to provide challenges, opportunities and requirements for top level basic and translational research.

If the HHMI TB research institute in Durban develops in isolation from the TB research excellence that is already present in S. Africa, a great opportunity for access to cutting-edge technology, core technical expertise and other resources will be lost. These include the next generation of “-omics” technologies (proteomics, metabolomics, etc.) and their required bioinformatics expertise. We note the willingness of the CoE to engage with the HHMI institute to assure their success and integration in the TB research activities in S. Africa.

Threats: Failure of long-term vision for core funding threatens the development of the next generation of junior and mid-level investigators. This is particularly critical because the senior PIs are coveted candidates for many other prestigious national and international posts. There needs to be support for core cutting edge equipment and technology with technical support staff, allowing continued competitive research at the highest international level. The
administrative burden and excessive oversight sap the energy and time of the CoE leadership and threatens to reduce the effectiveness of this critical core funding.

**Education and Training**

*Strengths:* MSc, PhD and postdoctoral training and track record have been excellent. The CoE has exceeded its targets for gender and met the black student target (see Appendix III). Students and postdoctoral fellows alike all reported satisfaction and deep gratitude to the faculty and staff for access to excellent equipment, top-up of bursaries, travel opportunities, a rich training environment, high quality research supervision, and international travel for research and conference attendance. Nearly all MSc students expressed the hope to continue to do a Ph.D.

*Weaknesses:* There is a lack of career development and career counseling for trainees and young faculty. Both research groups are somewhat isolated physically and academically from the larger institutions they are part of, risks to limit the exposure of trainees to the broader aspects of biomedical research and career opportunities.

*Opportunities:* Greater inter-nodal collaboration, for example around mutagenesis work in *M. tuberculosis* represents an opportunity for growth. Greater integration of the outstanding CoE research nodes within the larger biomedical research community of their parent institutions would promote greater exchange of students and faculty and thus enrich the impact of the CoE in TB research. Increased exchange could occur through rotations or longer exchange of students between nodes of the CoE, or increased North-South and South-North exchange for gaining analytical skills in bio-informatics, statistics, etc., i.e. technology and skills not readily available in S. Africa.

*Threats:* The relative isolation of the nodes of the CoE may limit access to pools of trainee candidates in particular for the S. African students. The target of a 2 year Masters degree and a 3 year PhDs limits the depth and quality of the research experience. This target requires constant training of new students by senior investigators and thus limits the number of students that can be trained because of lack of mid-level and junior investigators. The lack of clear career paths beyond a narrow focus on the academic track with limited posts for research may limit future interest of students to pursue a career in biomedical science research.

**Information Brokerage**

*Strengths:* The CoE’s research has had a direct impact on national and WHO policy on management of drug-resistant TB. This is a major accomplishment. Both nodes are actively involved in the sharing of knowledge amongst researchers within the CBTBR through lab meetings held at least weekly, where a hands-on approach is taken in assessing results and discussing lab-based problems. Journal Club meetings, held weekly at both sites, also provide the sharing of broader-based scientific issues and ideas within the field of biological sciences. The IT services of the respective host institutions have provided a high level of service and security with selective authentication to databases on a LAN and knowledge is made more accessible to staff and students by provisions of computers, laptops
and network points to the facilities and regular software updates. The CoE interacts with the scientific community by conference presentations and publications, as discussed above. The CoE has seen its findings translated to stakeholder groups such as policy makers and healthcare service providers, and to a lesser extent the health consumer in one important area: management of drug-resistant TB.

**Weaknesses:** The Nuggets prepared by the CoE and regularly reported to the DST/NRF are not passed on and disseminated.

**Opportunities:** Becoming increasingly active in meeting with and presenting latest research results to the City health department (Cape Town), the NHLS, the Western Cape Government (Dept. of Health) and the National Dept. of Health on occasion represents a great opportunity. The MRC Corporate office’s offer offered to prepare policy briefs or any other document required to move research towards translation, and to arrange briefings of relevant Parliamentary Portfolio Committees also is a great opportunity. Enhancing academic exchange within nodes and within each respective university represents another opportunity to make the excellence of the CoE more widely known within the institutions within which they operate.

**Threats:** Information brokerage is an important and laudable activity. However scientists are not optimally skilled in this area and too much effort spent without adequate professional support, through the CoE or the Universities with which the nodes are associated, will reduce effort by senior investigators in the primary missions of research and training excellence.

**Networking**

**Strengths:** The CoE has an extremely broad and impressive network of top international collaborators as manifested by joint publications and funding from international organizations. Whereas there are many US and European collaborators, there are also collaborations with other leading universities and investigators in Sub-Saharan Africa, such as through the Grand Challenge Project (GC-6) that involves 7 sites in Africa and in which investigators at Stellenbosch have a leading role. Extensive and detailed listings of these collaborations and grants can be found in the document “Self-evaluation report by the CoE” in Sept. 2008.

**Weaknesses:** The collaborative network is largely international and will likely expand within S. Africa as more TB research is developed in the country.

**Opportunities:** There is an urgent need to integrate the planned massive expansion by the Howard Hughes Medical Institute (HHMI; USA) at KwaZula Natal University (KZN) in TB research with the goals and objectives of CoE to enhance access to technology, for career development for CoE trainees and transfer of CoE expertise for the success of the HHMI enterprise. Involvement of the CoE with the development of the HHMI institute in Durban represents a great opportunity where the NRF/DST can help assure integration with CoE activities and expertise.

**Threats:** Increasingly, large networks for TB research are being created, similar to what has already developed in the HIV field, largely driven by international funders looking to establish
sites for clinical and translational TB research in endemic settings. Participation in these networks can provide great opportunities for research but also run the risk of having research agendas imposed by outside investigators. The CoE is ideally poised to be an equal partner and active leader in such networks and with long-term core funding from DST/NRF supporting research in a TB endemic country, CoE investigators will continue to be sought as leaders and equal partners in these large TB research networks.

**Service Rendering**

*Strengths:* There has been extensive service rendering. Activities include facilitating the establishment of a collaborative link between the NHLS and the Geneva-based Foundation for Innovative New Diagnostics (FIND), provision of technical/scientific services to the Western Cape Provincial Health Department, the gold mines, Tygerberg Hospital and various TB clinics, the provision of advice and assistance to individuals, research groups and institutions, locally (including NHLS) and abroad, committee membership and scientific review work at the institutional, regional, national and international levels. Members of the CBTBR played advisory and participatory roles in the national and regional responses to the extensively drug-resistant (XDR) TB crisis. Assistance to SAN-Parks and Cape Nature regarding TB in wild animals has been given, and to the AACl for companion animals. The SU node assists the MRC (Delft) and SAAVI with infection problems in their animals. Both nodes have extensive experience with setting up, running and safely administering facilities and have lend their expertise to others in their institutions and beyond in need of setting up BSL3 facilities, most for clinical work. EBA work (drug trials)

*Weaknesses:* None.

*Opportunities:* Expanded interaction with undergraduates at Stellenbosch University and University of the Witwatersrand may improve recruitment of promising young honors students and reduce the isolation of the nodes of the CoE. As mentioned above, consultancy by the CoE to the HHMI institute being developed in Durban would greatly enhance its success and integration within the S. African TB research community. This consultancy would also be available to other S. African universities seeking to invest in TB research.

*Threats:* Rendering service is an important and laudable activity. However scientists are not optimally skilled in this area and too much effort spent without adequate professional support, through the CoE or the Universities with which the nodes are associated, will reduce effort by senior investigators in the primary missions of research and training excellence.

**Management**

*Strengths:* There is strong administrative integration and synergy between the two nodes. There has been optimal utilization of the human and financial resources by taking full advantage of the flexibility that core funding provides to leverage it successfully for additional funding and developing new projects.  

*Weaknesses:* There are too many reports to be written and there is micromanagement from central administration of the fiscal aspects of the CoE. And at times single-minded focus on
the demographic distribution of students has obscured the extraordinary achievements of this CoE.

**Opportunities:** Given the demonstrated excellence and success of this CoE in exceeding the DST/NRF’s criteria for success with a very limited budget that has been used and administered judiciously, increased investment in this CoE will allow immediate expansion of research scope, training and outreach.

**Threats:** A lack of commitment for long-term funding will affect the ability to offer MSc and PhD training positions beyond year 8.
Appendix I (Adapted from “Self-evaluation report by CoE” 9/08)

List of Articles in peer-reviewed journals from Sept ‘04 through June ‘08 (N = 112)

2004 (Sept-Dec)

2005

2006


2007

2008 (Jan-June)


90. Djoba Siawaya JF; Bapela NB; Ronacher K, Veenastra H, Kidd M; Gie R; Beyers N; van Helden P; Walzl G. (2008) Immune parameters as markers of tuberculosis extent of disease and early prediction of antituberculosis chemotherapy. J. Infect. 56:340-347. (IF=2.037)


103. Parsons S;Smith SGD; Martins Q; Horsnell WGC; Gous TA; Streicher EM; Warren RM; van Helden PD; Gey van Pittius NC. (2008) Pulmonary infection due to the dassie bacillus (Mycobacterium tuberculosis complex sp.) in a free-living dassie (rock hyrax - Procavia capensis) from South Africa. Tuberculosis 88:80-83. (IF=3.425)


105. Rustomjee R, Lienhardt C, Kanyok T, Davies GR, Levin J, Mthiyane T, Reddy C, Sturm AW, Sirgel...


Books/chapters in books (13)


Germany, ch. 3, pp. 53-69.


Non peer-reviewed articles (9)


Appendix II (Adapted from “Self-evaluation report by CoE” 9/08)

Summary of Publications, Impact Factors, and other outputs from the CoE

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<th>Publications</th>
<th>2004 (Sept-Dec)</th>
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<th>2006</th>
<th>2007</th>
<th>2008 (Jan-June)</th>
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<td>17</td>
<td>27</td>
<td>29</td>
<td>30</td>
<td>112</td>
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<td>Impact factor &lt; 2 a</td>
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<td>4</td>
<td>9</td>
<td>4</td>
<td>9</td>
<td>31</td>
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<tr>
<td>Impact factor between 2 and 5</td>
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<td>7</td>
<td>14</td>
<td>20</td>
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<td>Impact factor &gt; 5</td>
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<td>6</td>
<td>4</td>
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<td>Books/chapters in books</td>
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<td>3</td>
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<td>Non-peer-reviewed articles</td>
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a. IF = SCI impact factor
Appendix III (Adapted from “Self-evaluation report by CoE 9/08)

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<th>Education and training outputs</th>
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<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
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<td>43</td>
<td>47</td>
<td>56</td>
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<td>S. African postgraduate students (% of total)</td>
<td>23(82)</td>
<td>34(79)</td>
<td>36(77)</td>
<td>51(91)</td>
<td>50(88)</td>
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<tr>
<td>African postgraduate students (% of total)</td>
<td>3(11)</td>
<td>4 (9)</td>
<td>6 (13)</td>
<td>4 (7)</td>
<td>5 (9)</td>
<td>-</td>
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<tr>
<td>Foreign postgraduate students (% of total)</td>
<td>5(18)</td>
<td>9 (21)</td>
<td>11(23)</td>
<td>5 (9)</td>
<td>7 (12)</td>
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<td>Women students (% of total)</td>
<td>20(71)</td>
<td>27 (63)</td>
<td>31(66)</td>
<td>36(64)</td>
<td>37(65)</td>
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<td>Black students (% of total)</td>
<td>12(43)</td>
<td>14(33)</td>
<td>21(45)</td>
<td>21(37)</td>
<td>26(46)</td>
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<tr>
<td>Post-doctoral fellows (% of total)</td>
<td>5 (18)</td>
<td>9 (21)</td>
<td>11(23)</td>
<td>9 (16)</td>
<td>11(19)</td>
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<td>1</td>
<td>1</td>
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<td>1</td>
<td>9</td>
<td>1</td>
<td>14</td>
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<td>0</td>
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<td>1</td>
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<td>1</td>
<td>0</td>
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\( ^a \) Bursary and/or running cost and/or travel and/or other support