

# Center for Comparative Medicine and Translational Research External Review

College of Veterinary Medicine  
North Carolina State University  
August 20 – 22, 2008

An **External Review Committee** (hereafter called the Committee; see members on page 8) conducted a review of the Center for Comparative Medicine and Translational Research (CCMTR; hereafter termed the Center) at the College of Veterinary Medicine (CVM) at North Carolina State University (NCSU) on August 20-21, 2008.

Prior to the review, the Committee was provided with materials defining the Center's *organization, strategy, grants, events, service centers, training, collaborations, marketing, accounting, and self-evaluation*. The review's **agenda** is on page 9. There was an initial dinner meeting among the Committee; the Center Director, Dr. Gregg Dean; and Dr. Warwick Arden, Dean of the NCSU-CVM. A series of meetings were held the next day, beginning with Dr. Dean and continuing with Center core leaders and investigators, as well as CVM administrators. A final meeting was held with Drs. Dean and Arden on the last day of the review.

At the outset of the review, Dr. Dean provided a series of questions to be addressed by the Committee. These questions are answered, to some extent, in the overview and specific observations that follow. However, we have also included brief answers at the conclusion of the report.

## Overview

The Center was conceived by Dr. Jorge Piedrahita and other CVM faculty in 2004 to foster collaboration among faculty. Center designation was granted by the NCSU Board of Trustees in February, 2006. Faculty members from the CVM were invited to participate in the Center in September, 2005, and an organizational meeting was held in December, 2005. Dr. Dean was appointed Director in October, 2006 after a national search. Consistent with the original concept, the Center charter focuses on **opportunities for broader collaboration between clinical and basic science faculty**. Emphasis is placed on clinical research and graduate education in the veterinary teaching hospital. The charter also stresses the Center's potential role in development of the **Centennial Biomedical Campus**.

With formation of the Center, faculty joined one of **six research cores**: (a) *allergic diseases*, (b) *clinical genomics*, (c) *emerging and zoonotic diseases*, (d) *mucosal pathophysiology*, (e) *oncology*, and (f) *biostatistics*. These cores generally reflect the expertise of participating CVM faculty and ensure that all interested faculty have a "home." However, as indicated in the Self-Evaluation prepared for this external review, collaboration among faculty within the cores and resultant productivity vary considerably, suggesting the potential need for reorganization. Research cores are supported by **three service cores**: (a) *Clinical Studies*, (b) *Biosafety Level 3 (BSL-3) Biocontainment Facility*, and (c) *Flow Cytometry and Cell Sorting Laboratory*. The Clinical Studies Core arose from discussions among Center faculty and is now

supported by a five-year grant from Novartis Animal Health. Other cores were preexisting and “adopted” by the Center.

While **comparative medicine** and **translational research** feature in the Center’s title, the charter and initial mission statement do not emphasize human health or commercialization. Instead, opportunities to enhance collaboration between basic and clinical veterinary scientists to advance understanding of animal diseases are stressed. The subsequent **Strategic Development Portfolio**, developed in December, 2006, is intended to “foster and facilitate systematic development and innovation in the CCMTR.” This Portfolio includes a seven-point *vision* supported by key *strategic initiatives*. Importantly, the expressed *vision* places greater emphasis on translational research, although the predominant thrust still appears to be veterinary versus comparative. Much greater emphasis is placed on the concepts of *one medicine* and *translational research* in the Center website (<http://www.cvm.ncsu.edu/ccmtr/>).

Given the original Center concept, most participating faculty are from the CVM. All but the biostatistics research core are centered there. Several faculty from the central NCSU campus participate, and there is considerable interest in involving others from both NCSU and universities/institutions in the research triangle area. The ability to include these individuals and enlist corporate support will markedly influence the Center’s success in conducting comparative and translational research.

Driven by both the **collaborative spirit** engendered by the Center and the initiatives espoused in the Strategic Development Portfolio, considerable progress has already been made. Of particular note, Novartis Animal Health has provided support for the new Clinical Studies Core, and a T32 proposal entitled *Comparative Medicine and Translational Research Training Program* has been funded by NIH/NCRR. This grant will provide six graduate student training slots, with two more supported jointly by NCSU and the CVM.

### Specific Observations

1. Several external factors provide special synergy and relevance for the Center:
  - (a) The **NIH Roadmap for Biomedical Research** (<http://nihroadmap.nih.gov/>) emphasizes interdisciplinary research and public-private partnerships. New funding opportunities, such as U-series grants, encourage “bench to bedside” innovation.
  - (b) As an outgrowth of the NIH Roadmap, the **Clinical and Translational Science Awards (CTSA’s)** will fund a national consortium of institutions intended to *transform the discipline of clinical and translational research* (<http://www.ctsaweb.org/>). Duke University and the University of North Carolina-Chapel Hill (UNC-CH) have received CTSA’s. The UNC-CH CTSA includes funding for training and pilot projects to be conducted in collaboration with the Center.
  - (c) The **NCSU Biomedical Centennial Campus** offers an ideal venue for translational research (<http://www.cvm.ncsu.edu/research/biopark/centbiocampus.html>). In principle, participating companies will be able to take advantage of clinical and basic research conducted through the veterinary teaching hospital and bench laboratories of Center faculty. In turn, animal patients will be the first to benefit from new discoveries and associated preclinical and clinical studies.
  - (d) The new **Randall B. Terry Jr. Companion Animal Medical Center** (<http://www.cvm.ncsu.edu/construction/>) will accentuate opportunities for clinical and

translational research. This should further enhance the capability of clinical faculty to attract and evaluate animals with spontaneous (naturally-occurring) diseases, allowing definition of potential valuable models of analogous human conditions and ensuring better case accrual for clinical trials.

2. The Center enjoys near uniform support among participating faculty and administrators. This, undoubtedly, relates to the *bottom-up* manner in which the Center was developed and the conscious effort to include all interested faculty. Thus, as the Center naturally evolves and matures, with some associated contraction and/or expansion, care should be taken to be open and inclusive in all deliberations.

3. While participating faculty are mostly supportive, some key individuals apparently have chosen not to participate in any research core. This may be due to a lack of synergy with the focus areas or lack of interest in the center mission or approach. We sensed that this may be particularly true of the oncology research core. With the evaluation of the existing research cores this Fall (see further below), a renewed effort should be made to engage faculty.

4. For the Center to be successful, it will be important to **define success** and enlist **broader financial support**. With regard to the *definition of success*, the term *translation* must be defined. In particular, is research being translated to animals, humans, or both? In our minds, translation should include both animals and humans. Given the translational research focus, one logical source of additional funding will be biomedical companies, particularly those with a presence in the research triangle area. However, currently, there is no readily apparent reason for them to become involved. Care should be taken to better define key components of the Center that will facilitate translation and commercialization. The *translation* and *application* bullet points on the website provide a framework. Two, albeit still developing, models are the **Cambridge Molecular Therapeutics Program** (<http://www.hutchison-mrc.cam.ac.uk/cmtp/index.html>) and the **Oregon Translational Research and Drug Development Institute** (<http://www.otradi.org/company.htm>).

5. The Center Charter indicates that research cores are to be reviewed every 5 years. An evaluation is planned for this Fall. Criteria for evaluation detailed in the charter primarily speak to evidence of collaborative research (joint publications and grants), with no mention made of translational research (industry contacts, clinical trials, potential for investigational new drug [IND] applications, etc). These same criteria are to be used in judging potential new research cores. Consideration should be given to redefining these criteria to better reflect the translational research mission of the Center.

6. Strategies to more fully engage faculty/investigators from the main NCSU campus and research triangle area must be carefully considered. Ideally, this group should include representatives from medical schools and industry, so as to better address the comparative and translational research missions. Essentially, teams of researchers that include physicians should be developed to ensure translation to humans. Ongoing collaborations between Center/CVM faculty and scientists and physicians in the research triangle area would be the logical bridge to involve them, i.e. one-on-one discussions initiated by Center/CVM faculty, participation in the Center seminar series, etc. With regard to the main NCSU campus, we were impressed with the passion for collaboration demonstrated by faculty and Dean Blanton (Blan) Godfrey from the College of Textiles. **Strategies should be developed to encourage even broader participation by NCSU faculty**, i.e. shared faculty recruitments (leveraging existing funding), restricting pilot project funding for several rounds to initiatives that include NCSU physical science faculty, ensuring that NCSU faculty on the main campus are aware of Center training slots and encouraging joint graduate student mentorship,

inclusion of additional research and/or service cores that are principally based on the main campus, etc.

7. By definition, service cores should *add value* to a Center. The developing **Clinical Studies Core** promises to facilitate collection of important data from clinical patients and serve as a biospecimen repository. However, based on the rate of current sample collection, there does not appear to be uniform acceptance among Center faculty. This problem will likely be addressed, at least partially, by the new Clinical Studies Core veterinarian. In the interim, further efforts should be made to bring faculty on board. As one example, faculty could be encouraged to use the services of the Core as part of the hospital approval process for clinical trials. It will be important for the Clinical Studies Core to obtain feedback from all users to continually improve service and identify any areas of inefficiency. Speaking more generally, each of the cores should have a business plan that takes into account existing and potential funding and provides users with a service level agreement so that they know what to expect. By definition, service cores usually do not make a profit. Most require ongoing support from the parent organization, in this case either the Center or CVM. Thus, each core should be carefully considered and justified based on service provided to Center faculty and the potential to offset expenses through other sources, to include service fees. Based on results from the January, 2008 survey and our discussions with faculty and staff, the Flow Cytometry-Cell Sorting Core is being used relatively frequently and, presumably, is generating reasonable service fees. On the other hand, the BSL-3 laboratory is underutilized, in part because of difficulties in filling faculty lines in the recent infectious disease cluster recruitment. As to additional cores, we feel that careful analysis must be completed before duplicating services already provided at NCSU or within the research triangle area. With this said, several other cores could add value to the Center. Perhaps, most obviously, support for routine **biostatistical analysis** is needed, potentially through assignment (with appropriate salary support) of an instructor-level biostatistician. We also feel that an **imaging core** would provide important biomarkers that could be used in preclinical and clinical studies. This would, naturally, take advantage of existing CVM expertise in diagnostic imaging (<http://www.cvm.ncsu.edu/vth/radiology.html>), to include the Iams Pet Imaging Center, and could be done in collaboration with imaging cores elsewhere in the research triangle area, such as the UNC-CH Biomedical Research Imaging Center (BRIC) (<http://bric.unc.edu/>). Other cores (cardiology, physiology/function, electrodiagnostics, etc) could evolve from existing clinical services in the veterinary teaching hospital. Diagnostic techniques offered from these **clinical cores** undoubtedly already serve as valuable biomarkers for clinical trials being conducted throughout the teaching hospital. From a broader perspective, consideration could be given to approaching NCRR regarding prospects for developing a **large animal reagent core**.

8. For the Center to achieve maximal visibility and better meet the needs of the state's animal-owning public, strategies should be explored to more proactively involve both animal owners and practicing veterinarians. Importantly, this will ensure that relevant problems are being addressed and also facilitate case accrual for clinical trials. As detailed in the service core section, the existing Clinical Studies Core already embraces this concept, with its stated goal "to expand collaborative relationships beyond the university with practicing veterinarians, animal owners, and industry partners." This mirrors an overarching goal of the CTSA initiative discussed earlier "to engage communities in clinical research efforts." Additional strategies could entail inclusion of practicing veterinarians and animal owners on Center advisory groups, wide

circulation of seminars, focused presentations to practitioner and/or animal owner groups, etc.

9. Several **programmatic gaps** were identified. We have already discussed the need for biostatistical support and greater buy-in among faculty for the Clinical Studies Core. In addition, as with most universities, there is a shortage of housing for large research animals, including dogs and cats. The lack of BSL-3 animal housing is a more specific need that will likely limit development of the *Emerging and Zoonotic Diseases Research Core* and utilization of the BSL-3 service core. Mechanisms to address research animal housing go well beyond this report and will require involvement of administrators within the CVM, NCSU, and, perhaps, the research triangle area. One starting point would be to commission a needs analysis, in the short and long term, together with a master plan for meeting the identified shortages.

10. Plans for the Center, particularly new initiatives, should mesh with and complement the CVM and NCSU strategic plans. These plans should be referenced in Center materials.

### **Specific Written Questions Addressed to the Committee by Dr. Dean**

#### **1. Has the leadership of the CCMTR been effective in accomplishing the mission?**

The CCMTR mission espoused in the original charter was to “enhance collaborative, interdisciplinary approaches for the comparative study of the molecular aspects of animal diseases” and, in particular, “to strive to support interactions between the clinical and basic research groups within the College of Veterinary Medicine (CVM) and the university community ....” The Center has definitely enhanced collaboration among CVM faculty and, to a lesser extent, those on the main NCSU campus. Moreover, there are clear examples where interdisciplinary efforts arose from Center visibility and activities. A notable example is the **avian ovarian cancer project** that led to funding of a NIH K25 grant (*Comparative proteomics applied to the avian model of ovarian cancer*, Hawkridge A, Principal Investigator). As detailed above, since the original Center charter was developed, the mission has evolved appropriately to include greater emphasis on the comparative aspects of human diseases and translational research. Goals associated with this expanded mission will, inherently, be challenging and call for concerted leadership. (Also see Specific Observations 4-6, 8, and 9).

#### **2. Has the membership benefitted and been sufficiently engaged in the Center?**

As discussed at multiple points during the review, it is difficult to define *benefits* that were derived directly from the Center versus those that would have occurred anyway. With this said, the Center can legitimately take pride, and claim success, in/for several key initiatives. Three of the more notable examples are highlighted here.

a) The **Clinical Studies Core** arose directly from discussions among Center faculty and the perceived “desperate need” for assistance with clinical trials and sample collection and storage. **Novartis Animal Health** recognized the powerful implications for this core and committed \$625,000 over a five-year period.

b) The **NIH T32 Training Grant** (*Comparative medicine and translational research training program*) [CMTRTP]; Dean G, Principal Investigator) capitalizes on the ability of

Center faculty to collaboratively train veterinary specialists in biomedical research, and, thus, help meet a critical national need.

c) The **avian ovarian cancer project** (NIH K25 grant [*Comparative proteomics applied to the avian model of ovarian cancer*, Hawkridge A, Principal Investigator]) arose directly from discussions among Center faculty at the initial organizational meeting. (Also see Specific Observations 2 and 3 for input on faculty engagement in the Center).

### **3. Has the CCMTR added value to the CVM and NC State?**

As discussed above, the Center has already added value in building a collaborative spirit among faculty and through several key initiatives. However, suffice to say, the greatest value of the Center, particularly relating to translational research, is still to be realized. (Also see the response to Question 2 and Specific Observations 4, 6, and 8).

### **4. The CCMTR was established on a common research philosophy rather than specific research topics. Should there be an effort to bring common research focus to each of the research cores?**

To be true to the Center's mission, the overarching common research focus should be the potential for commercialization of discoveries that advance diagnosis and management of diseases affecting both animals and humans. (Also see the response to Question 2 and Specific Observations 4 and 5).

### **5. The initial approach with Center membership was to be inclusive. It was anticipated by the original steering committee and executive committees that there would be a need for membership contraction and this would be accomplished through a membership review process that is scheduled to occur Fall 2008. Should the CCMTR limit membership and if so what should be the basis of selection/elimination?**

There is no *easy answer* to this question. The Center's proactive effort to be inclusive has engendered good will. Any decision to "contract" or expand the membership (or research cores) should be done through an open and inclusive process. This discussion will occur naturally during the Fall, 2008 review. For sake of **individual membership**, Center charter designation of criteria for *full* and *associate* members provides a means to single out engaged people. Full members should be actively and productively engaged in one or more research cores. This could facilitate group discussions and decision making. With regard to evaluation and selection of **research cores**, greater importance should be given to criteria that substantiate translational research (industry contacts, clinical trials, potential for investigational new drug [IND] applications, etc). (Also see Specific Observations 2 and 5).

### **6. An important objective of the CCMTR is to develop partnerships with corporate entities. What are the specific attributes, programs, or elements of the CCMTR that could be leveraged through academic/industry partnerships?**

Industry could be involved on at least three levels in the Center, namely the **discovery phase** for drugs/vaccines and diagnostics; **pre-clinical studies** for human therapeutics; and **clinical trials** for animal therapeutics. As discussed by Dr. Everitt during the

review, there has been a trend in the pharmaceutical industry to form novel industry-academic alliances and partnerships to virtualize drug discovery and externalize aspects of drug development. As one example of this new opportunity, GlaxoSmithKline recently forged academic partnerships to develop alternative drug development models (<http://www.admin.cam.ac.uk/news/dp/2008072504>). Thus, industry might initially be involved with Center basic scientists during the discovery phase. Once candidate therapeutics have been identified, industry could conduct pre-clinical studies in animal models, with a view to ultimately market the treatment for human use. In this context, Center programs that include well-defined animal models analogous to human diseases would be particularly attractive. Finally, veterinary pharmaceutical companies may choose to conduct clinical trials on animals with certain diseases. For both preclinical studies and clinical trials, the new Clinical Studies Core will be valuable. In addition, cores that offer quantitative **biomarkers** to judge therapeutic efficacy would be useful. This is a principal reason that we have highlighted the potential value of an imaging core. (Also see Specific Observations 4 and 5).

**7. What additional service cores would most benefit the research efforts of the CCMTR?**

(See Specific Observation 7).

**8. What are the specific strategies that could be pursued to fund service cores?**

With regard to overall Center funding, the major **governmental, industrial, and philanthropic** funding sources are being pursued. Specific strategies need to be developed to fully capitalize on each. Of course, most importantly, the Center must be perceived as relevant to the needs/goals of the particular funding agency or donor. From the vantage point of translational research, the Center should continue to engage practicing veterinarians and industry. One potential strategy would be to appoint special advisory groups from both industry and private practice or a joint committee. Many centers derive income from either indirect costs or salary recovery off grants that originate within the center. This could become possible as the Center matures but seems impractical at this point. Speaking specifically about the cores, subsidy funding should come from both the college and departments. This will help assure that cores are relevant to faculty needs. Individual budgets should be developed to show sources of revenue, all costs, and subsidy funding. Subsidy levels, budget models, and fees should be reviewed yearly. Service cores should produce annual reports that include financial statements, level of use, and user feedback. The college fiscal office should help the centers with reporting and budgets. As discussed earlier, the Flow Cytometry and Cell Sorting Core likely is deriving considerable income from user fees. In contrast, the BSL-3 laboratory appears to be supported principally through the central CVM budget and the Breitschwerdt laboratory. Just as with the overall Center budget, the service cores must be seen as relevant to receive funding. **Service fees** derived from grants of individual Center faculty are the most logical source of income. Support for cores to include salary and subsidies for participating investigators can also be incorporated into larger grants such as program project grants. Industry would be inclined to support cores that provide biomarkers for clinical trials. (Also see Specific Observation 7).

## External Advisory Committee

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**Center for Comparative Medicine and Translational Research  
External Review Committee Agenda  
August 20-22, 2008**

**Wednesday, August 20<sup>th</sup>**

6:00PM Dinner at An, located at the Arboretum in Cary at Harrison Ave and Weston Parkway. Take the Harrison exit off of I-40 (Dean Warwick Arden, CCMTR Director Gregg Dean, ERC)

**Thursday, August 21<sup>st</sup>**

All meetings will take place in the CVM Research Building Room 256 except the Overview that will be in room 294

8:30-9:30 Overview-CCMTR Director Gregg Dean  
9:30-10:30 Research core leaders (Philip Sannes, Jorge Piedrahita, Jon Horowitz, Marie Davidian, Bruce Hammerberg, Gregg Dean)  
10:45-11:45 Dean Warwick Arden  
12:00-1:15 Lunch with assoc deans (David Bristol, Michael Davidson), CVM dept heads (Lizette Hardie, Chris McGahan, Malcolm Roberts), and external dept heads (Sastry Pantula, STATS; Todd See, AS) and Blan Godfrey, Dean Textiles  
1:30-2:15 Dave Green, Director of College Communications, and Kate Azizi, Director of Corporate and Foundation Relations  
2:15-2:45 Service Core staff (Kim Williams, Xandi Hamilton, Janet Dow, Barb Hegarty)  
2:45-3:15 Greta Johansen, Business and Finance, Asst Dean  
3:15-3:30 Break  
3:30-4:30 CCMTR faculty (Stefan Franzen, Bala Rao, Steve Suter, Natasha Olby, Sid Thakur, Frank Scholle)  
4:30-5:30 External Review Committee discussions  
6:00 Dinner at Fins, located at 110 E. Davie St, Raleigh (Sam Jones, Ed Breitschwerdt, Anthony Blikslager, Mary Tompkins, ERC)

**Friday, August 22<sup>nd</sup>**

9:00-11:00 Exit interview (ERC, Dean Arden, CCMTR Director Dean)