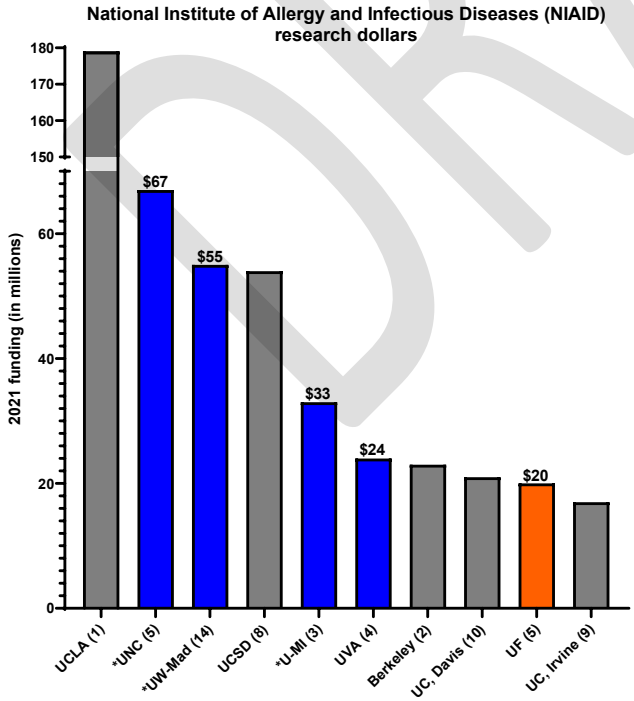
Research and Scholarship Council
Report to UF Faculty Senate Chair

Summary of facts related to Pathogen Research Improvement, IRB / EH&S Approval Efficiencies, IACUC Services

Pathogen Research Improvement

Biomedical research at UF is being limited by a lack of investment in infrastructure. UF Health has made significant investments in research infrastructure for basic clinical research. The most recent examples are the Clinical and Translational Research building and the Data Science and Information building which houses health-related research from the College of Medicine and the College of Pharmacy. Going forward, the UF Research Office and UF Health are in discussions on the construction of a new facility to increase biomedical research, including animal facilities.

Recruitment, retention, and reputation are all at stake because of the issues detailed within. Infectious disease is one of several specialized biomedical research areas in which UF has competitive programs. However, UF infectious disease researchers are at a huge disadvantage compared to our peer institutions, which creates missed opportunities to hire world class faculty and garner increased NIH funding. Underscoring this point, UF brings in substantially less NIAID dollars than our peer institutions:



Facility limitations and cost

- More ABSL2 rodent space is desperately needed. The new biomedical research building under consideration will include animal housing and research space. The college will need to prioritize what type of space will be included within the facility.

- Non-animal BSL3 space at EPI is completely full. Investigators with large NIH grants funding high-containment research cannot get more space and have had to resort to their lab members working in round-the-clock shifts. EPI is a unique resource that UF has within its portfolio. The fact that this resource is fully utilized speaks well to UF's ability to attract funding and researchers in this area. At present, UF does not have available funds to build a second EPI building.

- BSL-3 laboratories are used to study infectious agents or toxins that may be transmitted through the air and cause potentially lethal infections. It is our most intensely regulated and highly resourced research space. BSL-3 labs are the most expensive to construct and manage. UF is fortunate to have BSL-3 labs that can accommodate this type of research involving mice. At present, the number of UF faculty that require BSL-3 space for mice research is less than 10. For BSL-3 research using larger animals, significantly different and more expensive facilities would be needed. To date, UF has not elected to prioritize the construction of a new facility designed for BSL-3 research with larger animals.

- Inability to perform ABSL3 experiments on non-rodent models is an impediment to hiring and retaining world-renowned researchers. For example, UF researchers were denied requests to work with SARS-CoV-2 in pigs, hamsters, and cats early in the COVID-19 pandemic. These have all now been established by other universities as important model systems for understanding disease in COVID patients and testing antiviral drugs. Moreover, we have been unable to recruit multiple well-funded influenza virus researchers because we cannot provide them with ferret facilities.

- As stated earlier, UF has not elected to invest the significant funding necessary to construct and operate a BSL-3 facility suitable for animals larger than mice. It could be done, but it would be at the expense of other facilities and research needs on campus.

- A central portion of one of UF's animal facilities was renovated in 2008 to rodent ABSL3 space. It was specifically designed to support rodent work. Thus, UF does not have the infrastructure, equipment, or expertise to do "other" species. It can certainly be done but would take a significant investment of time and resources.

- ABSL3 per diems are far above peer institutions. UF per diems are at $11.91 per cage. This can be compared to U-MI per diems of $3.75; U-WA per diems of $3.48; and UAB

per diems of $0.75. However, these are not all entirely fair comparisons because the cost structures vary. For example, departments at U-MI with participating faculty pay operating costs of $41K per year and U-WA charges separately for PPE and room rental which is wrapped into UF's per diem. However, UF's per diems do still leave our PIs paying much higher total costs than our peers. Comments from UF faculty who work with ABSL3 pathogens underscore this point:

  - "It's made so difficult, costly, and slow that you just give up."
  - "The ABSL3 cost is literally oppressive."

- Large animal per diems are far above peer institutions.
  - "I am leaving UF because per diems for pigs are $25 per day compared to $4 per day at peer institutions."

  "I have had to drop large animal studies with BSL2 containment because of costs."

- UF has compared its per diems to other universities and found that non-UF departments or colleges also provide resources to support their ABSL3. The current UF ABSL3 facility is subsidized around 75%. By comparison, "routine" rodent research is subsidized around 30%.
- The ABSL-3 research is one of the most highly subsidized research areas on campus. We do so because of the importance of the work. The expectation is that externally funded proposals will include the subsidized per diem costs for the proposed research. The per diems are higher for ABSL-3 work than for animal research that does not require the ABSL-3 facilities and procedures. This simply reflects the realities of costs.
- UF's current basic swine per diem is $12.68 while the advanced rate is $20.95. U-IO is $30.18, U-CO, Boulder is $35.98, U – Rochester Medical Center is $56.59, U of WA is $42.62. A wide range of per diems exist and as stated for ABSL3, these are not entirely fair comparisons since there are many variables associated with the per diems e.g. single vs. group housed, containment level, type of research work, etc.

Logistical limitations

- There is a regulatory requirement that BSL3 facilities require occasional closures for inspections due to the hazards associated with pathogen research, and to provide for equipment repairs. At UF, these occur annually and generally take 1 month at the EPI for non-animal BSL3 space and 1-3 months in the ABSL3 facility. At peer facilities these closures are typically one week. An example of a peer institution with much larger BSL3/ABSL3 facilities that has an annual 1-week shutdown is Colorado State. The lost research time for UF investigators that rely heavily on high-containment research is unsustainable and has led to the departure of successful faculty.

  - Comment from a Chair: "A junior faculty member's productivity has been hugely hampered due to shutdowns every year and now I'm nervous they will not get tenure."
- UF's average time for the annual shut-down is about 6-7 weeks. It went longer on 2 occasions because there were facility and infrastructure systems that did not pass the final validation tests and it took additional time to fix them. UF can do more to shorten the downtime but needs appropriate resources to do it (e.g. dedicated staff, overtime for staff and vendors, etc.).

Slow approvals

- Multiple PIs waited over 10 months to be given access to an ABSL3 suite to perform SARS-CoV-2 infection studies in a rodent model. Having animal access earlier would have elevated a project they were trying to get published and made them more competitive with their peers, many of whom had nearly immediate access to ABSL3 because their universities recognized the need to expedite this process in the middle of a pandemic.
  - There was a documented delay of 3-4 months, but this was still a long delay. It is a lengthy process to get final approval to work in the ABSL3 including writing SOPs, getting them reviewed by multiple parties, training PIs, getting them approved, etc. Due to staff attrition (low base pay for ACS staff), there was only 1 manager qualified to do this task but the manager is also responsible for overseeing the entire facility (small and large animals) in addition to the ABSL3. These delays are an issue of resources and priorities.
- The average time for EH&S to approve biosafety projects has increased from 10 days to 90 days over the past decade.
  - In recent months, the VPR has worked with EH&S leadership to allocate funding necessary for additional staff to address current bottlenecks in securing approvals
- The increase in EH&S staff is not proportional to the increase in research at UF over the past decade as the number of protocols have doubled without increasing staffing.
- IACUC and EH&S issues are creating concerns for UF faculty recruitment and retention.
- Slow approval process of BSL3 protocols and SOPs at the Biosafety Office (EH&S) as well as ABSL3 in Animal Care Services
  - The VPR has worked with EH&S leadership to allocate funding necessary for additional staff to address current bottlenecks in securing approvals
- EH&S Leadership at the R&S Council meetings advise that a review of peer university protocols would be helpful.

The combination of difficult and slow approval processes and extremely high costs have led to a perception among UF faculty that the university is risk averse and does not support infectious

disease research. This has led to the loss of talented faculty members and hurts our reputation, impacting recruitment. This perception was encountered repeatedly when interviewing PIs working in this space. Just a sampling of quotes collected over the past six months:

- "The vicious cycle of the inability to do this type of research at UF has driven most people to quit doing it or subcontract out."
- "It's made so difficult and slow that you just give up."
- "We desperately need more mouse space and everyone knows it, but administration refuses to invest in it."
- "I gave up on SARS-CoV-2 research because it was made so difficult here."
- "The reality is that UF is risk averse and incredibly slow."
- "The overarching issues is a pervasive unwillingness to be dedicated to this type of research. Do they want excellence in this field? I think not."

- ACS routinely compares the UF per diems to rates at other institutions. The subsidy provided by UF Research to ACS is the highest among all research operations on campus.
- There are some instances in which a specialized service is needed by a small number of researchers. In evaluating how to meet this need, UF examines the cost of setting up the service at UF versus the use of vendors or subcontracts with entities that reliably provide that service. Sometimes is makes sense to set up the service at UF, assuming that the user community will grow. Sometimes UF elects to subcontract.

Research and Scholarship Council Comment: UF faculty researchers feel that, compared with peer institutions, UF has severely limited ABSL2 and BSL3 space. Therefore, faculty researchers have the viewpoint that this is certainly a barrier to research. However, the R&SC was not made aware of any direct comparisons between the total BSL-3 space at UF as compared to other research universities. One issue is that UF has grown the research portfolio that utilizes these facilities. UF research is looking at how the user numbers can equate to upgraded infrastructure for this space. UF Research office recently allocated an additional $450,000 supplement for new caging and equipment for the ABSL-3 rooms. UF faculty researchers complain most about the unacceptable slow approval process for protocols. This seems to be due in part due to limited staffing.

UR IRB / EH&S Approval Efficiencies

- UF IRB procedures are not consistent with IRB procedures at other institutions.
    - Example:
        - UF IRB was approached in July 2020 with request for Public Health Surveillance Exception

- UF IRB requested we submit IMPACC as a study with full ICF and felt it did not meet the exception criteria
- After several meetings, Dr. Iafrate met with the PIs of IMPACC from NIAID to discuss the exception criteria. It was noted that UF would be the only site involved in IMPACC that would not grant the exception.
- Two other sites added IMPACC to already approved IRBs. They bundled the studies together
- Dr. Iafrate agreed to allow the exception, however if the intent was to store samples similar to the other sites, it would have to be under an IRB approved protocol with consenting for patient samples to be included in the repository. This specification caused several issues with the release of funding, since it sounded like a new IRB was being created for these residuals.
- Since IMPACC recruits participants who are COVID positive, hospitalized and, in some cases, intubated, it would be very difficult to consent these individuals for their samples on top of discussing the IMPACC study with themselves or family members. It was decided to not pursue sample storage.
- It was noted in the protocol that sites are allowed to keep residuals for their own research. This was one of the main issues Dr. Iafrate had with the study as he felt the samples would be unregulated at that point.

- The UF Human Research Protections Program, which includes the IRB, was recently granted full accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) which is the recognized industry standard. This accreditation includes the review of IRB policy and procedures. If UF IRB procedures were inconsistent with the industry standard, the AAHRPP review would have noted this. They did not.

- When UF researchers try to set up an sIRB for a multi-center project, the additional requirements for UF's IRB process can make it difficult for UF to serve as the lead institution. In some instances, delays of 8 months have been reported.
    - Example:
        - A UF study ceded to Duke University IRB per the sIRB guidelines. All recruitment material had been approved by Duke's IRB. However, the UF IRB requested language changes to the approved recruitment letter.
        - The only reason the letter was submitted to the UF IRB was to help clarify the enrollment process for non-consent2share

patients (a letter would be sent on the provider's behalf and then the coordinators would follow-up with a call).
- Although local context is allowable per the sIRB, however this situation set a precedent so that all recruitment material would need to be submitted to both IRBs, greatly slowing down enrollment. The recruitment letter would now need further approval from Duke for the new changes and then back to the UF IRB for final signature.
- When do recruitment materials approved by an sIRB need to be submitted to the UF IRB? Can/should the UF IRB make changes to the language that are not related to a state law or institutional policy?

- The single IRB (sIRB) process is a relatively new regulatory path for multi-institution human subject studies and has been a challenge for all institutions to implement efficiently. UF, like other institutions, are getting better at implementing sIRB studies.

- These workflows illustrate the current IRB and sIRB procedures:
  - IRB workflow
  - sIRB ceding to an outside IRB workflow

- UF IRB approves the study first to be conducted at UF, then other sites are added via revision later (which does not require full board review). Federal regulations require other institutions to sign an IRB Authorization Agreement (IAA). Using SMART simplifies that process, but UF cannot control how long it takes to execute these agreements (usually processed in a business day or two).
- Some issues brought before the Research and Scholarship Council have not been brought before the compliance units, and thus they have not had the opportunity to investigate or respond to some issues/allegations from faculty.
- UF IRB requires sign-off authority on studies that meet the published exempt guidelines and some faculty state this is not standard practice.
  - Many institutions require IRB review of exempt protocols because some researchers may misclassify research projects as exempt.
    - UF is actively exploring options to create a tool for automation/streamlining of this process.
- Additional funding has been allocated by Dr. Norton (12/21) for three additional staff members for EH&S/IBC. No additional staffing for IRB.
- Dr. Norton has convened two working groups involving multiple faculty to identify methods for improvement in IACUC and IRB operations.

  - Dr. Jennifer Bizon, Dept Chair of Neuroscience, CoM, and Dr. Lyle Moldawer, Professor in Surgery Dept, CoM, respectively are chairing these working groups. The IRB group has its first meeting next Tuesday February 8th. The IACUC group has not yet scheduled its first meeting.
  - Both groups are expected to publish results within 6 months and, if they determine an outside consultant is needed to assess our program, Dr. Norton has indicated we will pursue that.
- IRB and IBC Committees consist of faculty members.
- IACUC and IRB undergo external Accreditation, during which independent bodies assess our programs, review all of our policies and procedures, do file reviews, and visit campus to interview not only compliance committee members and staff, but also researchers and others involved in the research program. Both received full Accreditation with no major issues identified in early CY 2021.
    - IRB working Group Roster:
      Chair: Lyle Moldawer (COM)
      Azra Bihorac (ADR, COM)
      Rhonda Cooper-DeHoff (Pharm)
      Roger Fillingim (Dentisry)
      Jennifer Fishe (COM Jax)
      Duane Mitchell (COM, CTSI)
      Thom George (COM, Cancer Center)
      Peter Iafrate (IRB)
      Michael Mahoney (UF Research)

IACUC Services

IACUC ethics review of scientific merit and method

- Some UF researchers report that IACUC members have responded inappropriately by suggesting that some colleagues may be performing unethical experiments if they do not follow comments/suggestions by IACUC reviewers on scientific merit or study methodology.
    - The IACUC process is, in fact, an ethics review of proposed research involving animals. It is the duty of the IACUC to determine if the ethical standards as communicated in federal regulations are being met
- Some UF researchers report that previously approved studies can be disapproved simply because a new reviewer questions the methodology endpoints, although they are within standards for practice.

IACUC regulatory requirements for protocols with valid methods and scientific merit

- Some UF researchers have indicated concern about what they view as “mission creep” in IACUC reviews and have asked for another set of “checks and balances” to IACUC decisions.

- Some UF researchers state that the role of IACUC is not to help plan or execute experiments but to determine if practices are ethical and maintain animal welfare.
    - A better designed research study may utilize fewer animals or reduce unnecessary suffering. Therefore, the IACUC's primary mission may in fact have a role that impacts study design.
- Researchers indicated that new IACUC regulations can be implemented based on single non-replicated, publications.
    - Example:
        - Banning of Tribromoethanol (Avertin) even for terminal perfusion procedures. Avertin is nonpharmaceutical and not DEA regulated. All alternatives are pharmaceutical and regulated, adding a new layer of regulatory burden for what once was a very simple procedure.
- Researchers indicated that new IACUC regulations can be implemented without scientific evidence.
    - Example:
        - The requirement that USP grade drugs are used when available. No study was referenced to indicate hazards with non-USP grade chemicals.

IACUC approval logistics

- Researchers indicated there are inconsistent protocol reviews due to a lack of consensus among veterinarians serving on the review panel.
- Yes, we have recognized this and started an internal review process to provide consistency among veterinary review. In addition, moving to a new electronic system where PIs can develop libraries/templates that are permanent, once approved, will also help alleviate this concern.
- Inconsistent levels of expertise on IACUC panels.
- IACUC review period is too lengthy due to administrative process inefficiencies. (Three reviewers look at each protocol. A primary reviewer, vet, and EHS reviewer. Each review is done in series and not in parallel or with simultaneous committee meeting. Each reviewer has two weeks to examine the protocol. As a result, reviews with no revisions could take six weeks.)
    - Effective 2/1/22, all new studies and renewals are going into goIACUC – a vendor built system that was designed with input from and used by other universities. UF did not modify the workflow and it is standard practice to have veterinarians negotiate clinical issues in the study before IACUC review. EH&S was an issue and IACUC recently negotiated with EH&S to move this responsibility to the IACUC office in order to expedite/improve the timeline. In the old system, veterinarians and EH&S looked at the submissions not only **before** the IACUC review, but **after** as well. This contributed significant delays and IACUC no longer conducts the post review in goIACUC.
- Researchers view this as an excessive burden on investigators.

- Researchers also indicated that the IACUC mandated in-person classes are not offered frequently enough. New employees and students must wait to take classes before they can be added to protocols and before they can begin to participate in animal experiments/learn.
    - Currently, no backlog exists for these courses and there is availability within one business day.
- IACUC Committees consist of faculty members. Additionally, the IACUC Working Group is reviewing all IACUC and associated processes. The VPR encourages those interested to provide input directly to the working goup.
- IACUC and IRB undergo external Accreditation, during which independent bodies assess our programs, review all of our policies and procedures, do file reviews, and visit campus to interview not only compliance committee members and staff, but also researchers and others involved in the research program. Both received full Accreditation with no major issues identified in early CY 2021.
    - IACUC working Group Roster:
      Chair: Jennifer Bizon (COM)
      Erica Gonzaga (EH&S)
      Laura Eurell (ACS)
      Cheri Stabler (HWCOE)
      Dan Wesson (COM)
      Eric Krause (Pharmacy)
      Nancy Denslow (VetMed)
      Dan Brown (IACUC chair)
      Michael Mahoney (UF Research)

Research and Scholarship Council Comment: *A pervasive opinion exists among UF faculty researchers that IACUC and EH&S requires more oversight than what currently exists, and that IACUC staff actions during mandatory post-approval monitoring and procedure observation indicate that they do not trust UF faculty and researchers, and their actions seem demeaning and unhelpful. Additionally, compared with peer institutions, UF IACUC maintains overly burdensome procedures and requirements. The VPR encourages all interested parties to engage the IACUC Working Group with any concerns and suggestions.*

Research and Scholarship Council Conclusion: The majority of those who have presented their issues and provided comments to the Research and Scholarship Council suggest the most impartial and efficient process for examining these issues and developing a strategic plan to rectify problems is to create a process to benchmark UF with other peer organizations. Many faculty researchers feel this benchmark standard is best produced by an independent outside consultant group composed of faculty and staff from peer institutions. This consultant group would complete a comparative analysis of peer institutions on specific measures such as budget

analysis, staffing levels, required training and frequency, protocol volume, protocol review time, protocol review procedures, and IACUC review for merit and method. It should be noted that the IACUC Working Group exists. This group is comprised of faculty researchers and staff that can provide actionable recommendations. These may include process modifications, staffing needs, and other specific changes. It may also include recommendations to formally benchmark against comparable peers and/or to engage with an external consultant.