NIH S10 Proposals:
Tips for composing and submitting the strongest application
March 10, 2021

NIH S10 shared instrumentation grants are an important source of equipment funding for research cores. S10 grant writing is challenging: the format is complex and applications require integration of contributions from many colleagues. In this session, ABRF members, who have participated as reviewers in NIH S10 study sections and/or written successful S10 grants, will present tips for writing S10 applications and answer questions in a panel Q&A discussion.

Acknowledgements

ABRF 2021 S10 panel participants:

- Simon Watkins (University of Pittsburgh)
- Josh Rappoport (Boston College)
- Sherry Thornton (Cincinnati Children's Hospital Medical Center)
- Caroline Shamu (Harvard Medical School)

And, special thanks to Alena Horska (NIH ORIP) for answering many questions.

NIH S10 instrumentation grant program

- Administered by the Office of Research Infrastructure Programs (ORIP)
- Only one submission date a year, generally in late May or early June
- There are three funding levels/opportunities:
  - Basic Instrumentation Grant Program (BIG)
    - $25,000 -$250,000
    - This is a brand new program this year and is limited to institutions that have not received S10 instrumentation funding of $250,001 or greater in any of the Federal fiscal years 2018-2020
  - Shared Instrumentation Grant Program (SIG)
    - $50,000 -$600,000
    - This is the most commonly used mechanism
  - High-End Instrumentation Grant Program (HEI)
    - $600,001- $2,000,000
- More information and FAQ:

https://orip.nih.gov/construction-and-instruments/s10-instrumentation-programs

How many S10 grants get funded, and what about the duties of study sections?

- More than 500 S10 grants were funded over the last five years
- In FY2019, 407 applications were received and 130 grants funded (32%)
- S10 study sections fall into six broad categories of expertise, potentially with multiple study sections:
  - Biological Chemistry and Macromolecular Biophysics
    - Mass Spectrometers and NMRs (2 panels)
  - Bioengineering Sciences and Technologies
    - Computing
  - Cell Biology
    - Optical microscopes and tweezers, electron microscopes (standard and cryo), cell sorters (3 panels)
  - Genes, Genomes, and Genetics
    - Sequencers
  - Interdisciplinary Molecular Sciences and Training
    - Seahorse, laboratory automation/HTS platforms, SPR, ultracentrifuges, and other instruments (1 panel)
  - Surgical Sciences, Biomedical Imaging, and Bioengineering
    - PET, SPECT, CT, whole animal fluorescence, irradiators (1 panel)

- The number of study sections in each category varies annually, depending on the number of applications submitted, also some panels are quite large (optical microscopy) others quite small (electron microscopy)

These are SHARED instrumentation grants

- What's eligible?
- Shared!!!! Instruments
  - Several NIH-funded users
    - 3 minimum
    - The upper limit is soft particularly with institutional facilities. However, the description of the science has a page limit, so generally 8-10 research projects is a reasonable upper limit.
  - Cannot be a sneaky way of getting funding for a senior investigator and his/her buddies
    - The panel sees right through this type of application
  - The Science that the instrument will be used for is not being evaluated as the underlying grants have already been funded, however, the appropriateness of the requested device (and accessories) for the proposed use is in question. Know what you are talking about!

Important components

- **Do the applicants need what they are asking for?**
- Do the applicants have sufficient technical expertise?
  - Both to use the instrument effectively AND analyze the data that will be produced.
- Have they made a good choice?
- Will the instrument solve the problems being studied?
- Is the organizational/management plan good?
- Are plans in place for data management (access/storage/back-up)?
- Is the training plan well organized?
- Is the cost recovery viable and compliant with NIH guidelines?
- Is the institutional support sufficient to pay costs if there is a shortfall?

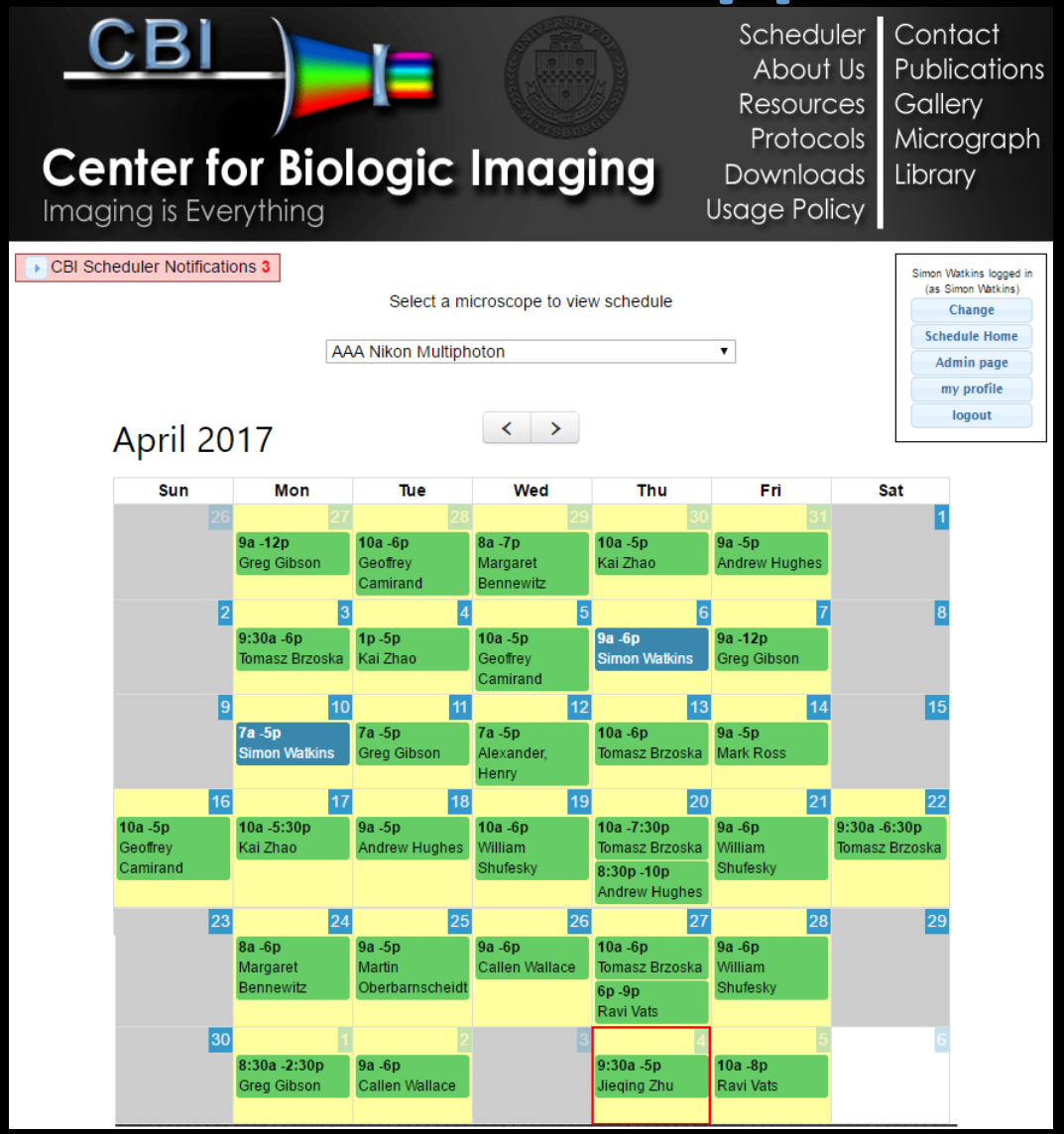
The Study Section Roster:

- Generally pulled from awardees and cognoscenti (including several people at this meeting!)
  - This means
    - Senior Faculty
    - Center Managers
    - Instrument Builders
    - Instrument Users
- What this really means is that the panel truly know what they are talking about and applicants really need to know their stuff!!!

First Triage Point: Need

- **Need, need need…** This is the first and most critical scorable criterion.
- There is a big difference between “want” and “need”. If you do not really need the system its probably going to be difficult to justify the request.
- You do not need to be asking for something cutting edge.
- As long as you can justify need:
  - Massively overused current devices
  - For example, this system is used more than 3000 hours/year

Example of need included in a successful HEI application from 2017



- Calendars showing use all day every day and at the weekend
- Emails, letters
- Use all the justifications you can to show what you have is over used.
- Or other features are needed
- Or what you have is no longer current

This may still not satisfy some reviewers and not all are equally knowledgeable as you may be

Overall Impact/Benefit: Dr. Watkins is requesting a Nikon A1R MPE resonant and galvo scanning microscope for shared use within the Center for Biologic Imaging (CBI). This is an unusual request because the CBI already has the same Nikon A1R. The main difference is that the new instrument will have two lasers for MPE. The enthusiasm for the otherwise excellent proposal is decreased because an almost identical instrument is available which is not fully utilized.

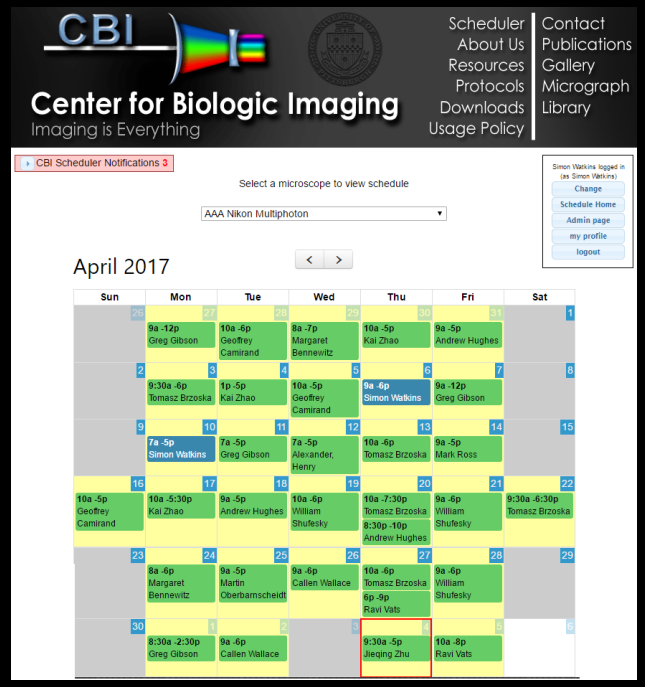
1. Justification of Need:

Strengths

- The Nikon A1R is requested because of near-saturation usage of the present instrument.
- The new A1R will have two lasers for MPE which will be useful for many of the NIH-funded projects.
- The PI has provided complete information on usage of the present A1R.
- The present A1R is used 2500 hours/year, which is 6.8 hours/day or 9.6 hours/5 day week.

Weaknesses

- The PI states that the present A1R is used at near saturation.
- The present A1R is not yet used at saturation levels.
- The need for two lasers could be satisfied by adding a laser to the current AIR MPE microscope.



- In this case 2500 hours was not considered saturation
- Fortunately the other reviewers did not concur

However, this is peer review which is a powerful thing.

Can I use this mechanism to replace old machines?

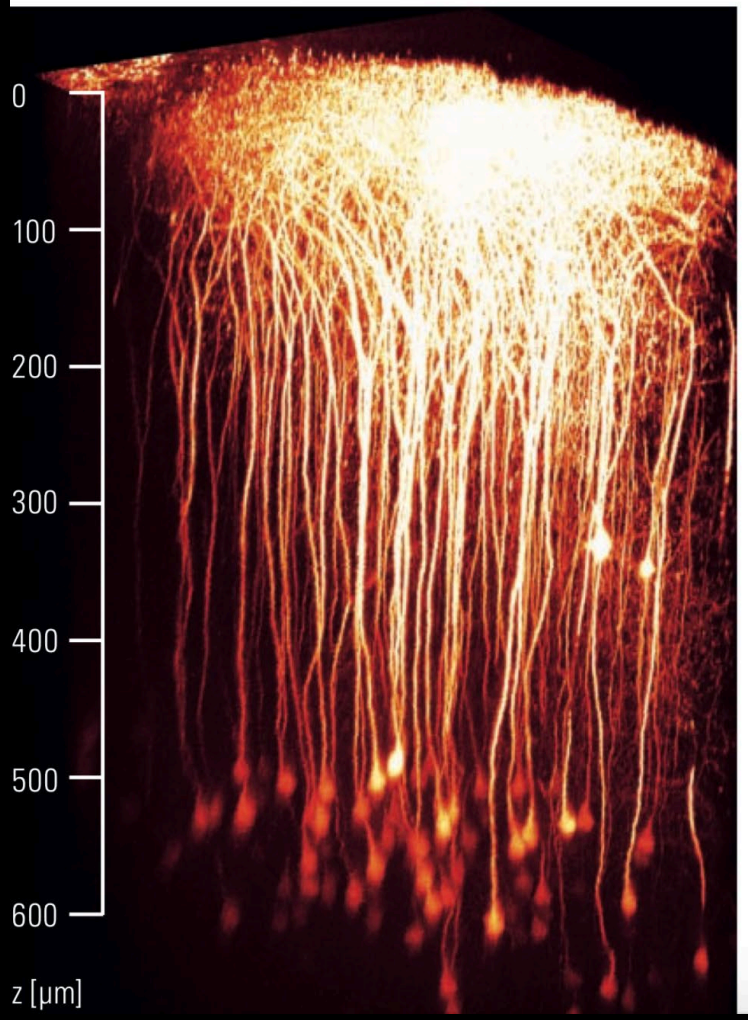
- Yes!
- So, how to justify this?
  - The best route is to get a letter from the manufacturer that categorically states that the instrument has reached end of life and can no longer be supported.
  - Remember that the panel will know what models are old and what is due for a replacement (they are experts).
  - If you complain that you need to replace a newer device because it is no longer working/working poorly, this really may just reflect a lack of maintenance and care for the device you have….. Not a good sign ☺

Second Triage point: Knowledge

- The panel is very knowledgeable… you need to know your stuff.
  - This comes out in the instrument comparison section
  - Opinion (why you prefer brand X over Y) is ok, but makes sure it is supported by knowledge, not hearsay

Knowledge is essential, this Means:

- Do not recite verbiage from brochures… for example…



LEICA TCS SP8 MP – YOUR PATH DEEP INTO TISSUES

Superior optics and detection for brighter, high contrast multiphoton images
New broadband anti-reflective coatings for scan optics and objectives provide highest transmission in the visible and infrared range for optimal excitation and detection. Leica IRAPO high-NA objectives are color corrected in the infrared up to 1300 nm to minimize the axial shift.

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More data in less time – largest field of view at highest speed
At 22 mm, the exceptionally large field of the Leica TCS SP8 allows large areas of tissue sections to be scanned in one go. Even at the highest possible speed using the 12 kHz scanner, there is no loss in resolution, sensitivity and contrast due to high-numerical aperture objectives with long free working distance of up to 2.5 mm.

Easy control from microscope software
For fast experiment setup, the microscope software LAS AF 3 provides full control of all motorized sliders and IR lasers including the prechirp unit. A wide range of additional software packages offers further functionalities, customized to your needs and always adapted to your latest applications.

Nifty things not to put in your grant application

- This is from my experience, as a microscopist: but really speaks to a limited knowledge base
- “We really need multiphoton microscopy because of its improved resolution over single photon confocal”
- “STED is very easy to implement with most available fluorophores and mountants”
- “Live cell STORM can be done readily with a “xxxx””
- Remember the Panel know their stuff….

Preliminary data

- This is not required, as defined in the program announcement from the NIH.
- In fact, the issue of a need for preliminary data in the application was a source of much discussion in the group as we prepared for this panel.
- HOWEVER "If an instrument can be demoed, including preliminary data is an effective way of showing advantages of the novel technology compared to what's currently available to the PI and the users." (NIH S10 program FAQ)
- Don't forget the science has already been judged, the point here is:
  - Does the group need it for the proposed science?
  - Can they use it expertly?
  - Does it actually solve the problem?
  - All preliminary data are good, even showing that a confocal helps over widefield… but for some justifications, it is essential….
- Most importantly only show really good powerful preliminary data that makes a solid and clear point.

Preliminary data is more important when pushing technical and methodologic barriers

- For example a few years ago we submitted a successful application for a 3 axis STED system.
- We included clear preliminary data for all 8 projects
- At this time STED was a new approach and we had to really prove its value.
- By the way this system is still producing exceptional data.

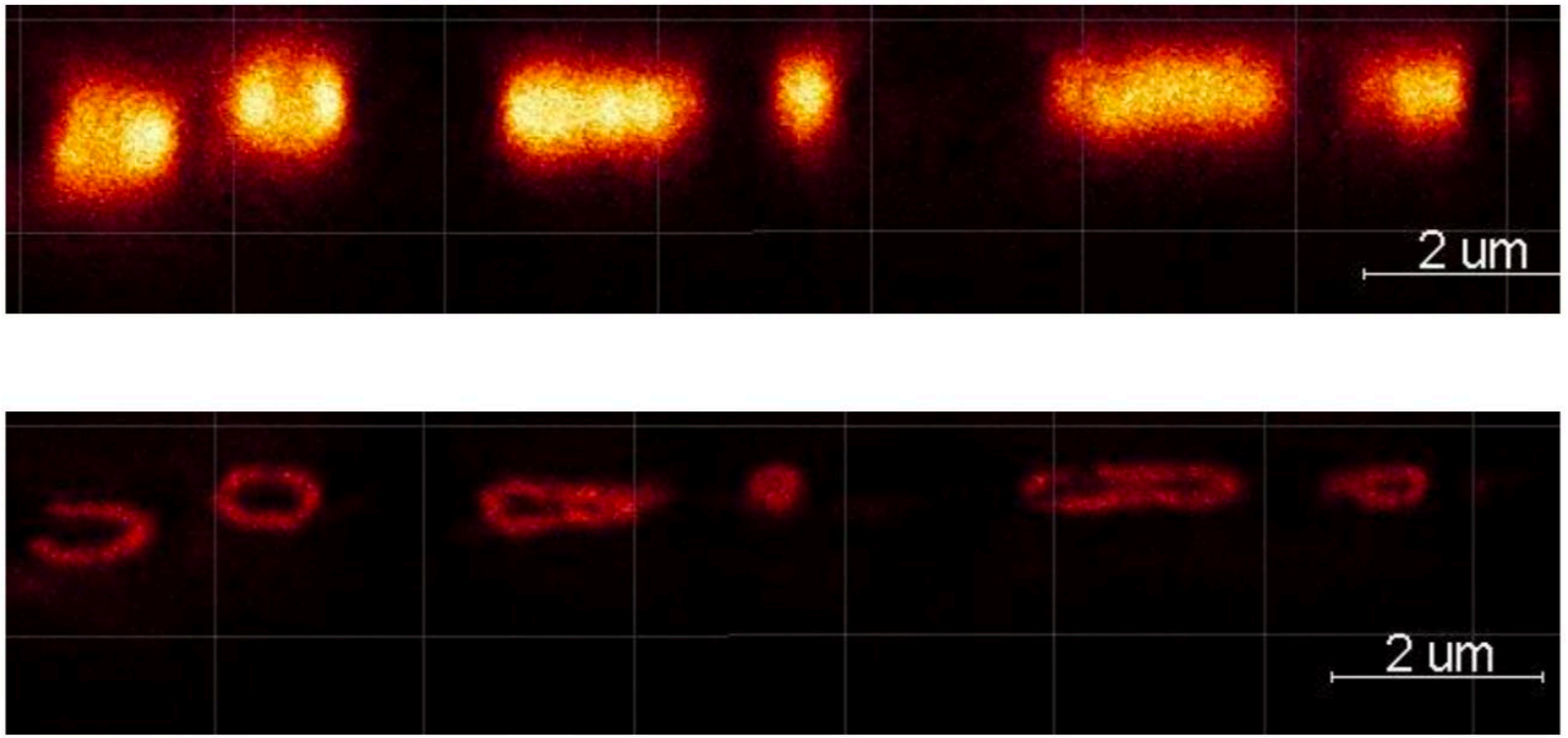


Figure 2: Comparison of Confocal versus STED imaging of TOM20 staining for outer mitochondrial membrane illustrating that the discrimination of sub organelle compartments are achievable using STED methodology.

Research Projects

- "Describe the benefit of the requested instrument to enhance Users' research projects".
- Generally this is around 1-2 pages/project
- Each project should mention the instrument by name and relate the need for instrument features to specific aims from the funded research grant.
- Don't simply paste text from the funded grant application into the S10.
- Edit project descriptions provided by Users so that all research projects are written in a similar style; templates can be helpful.
- The required user summary tables are important:
  - Major User projects
  - Minor User projects

Key information for each project

Grant details

Estimated # hours use/year

Estimated % of AUT use

Need for requested accessories*

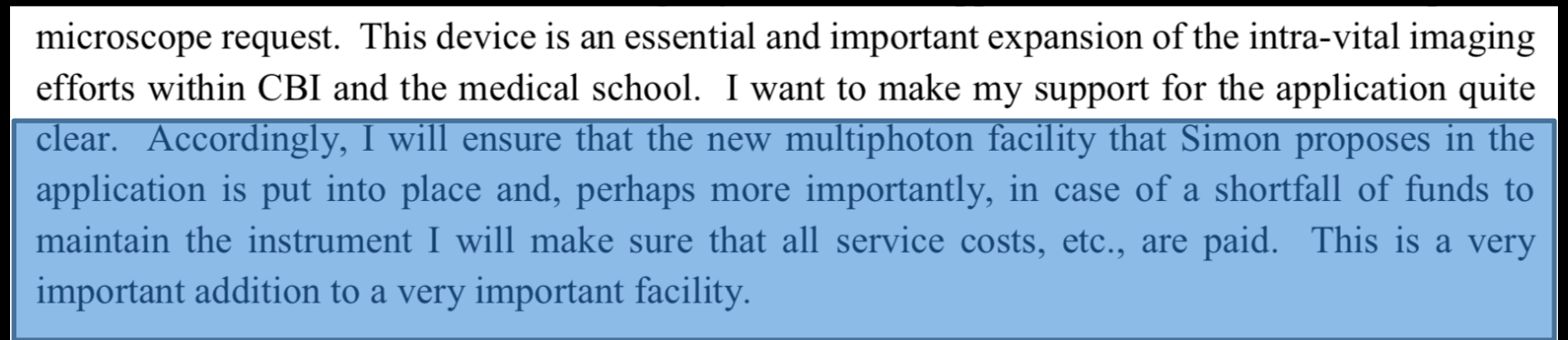
*Can be presented in a separate table

Management plan

- Do not short change this section, this is where it becomes clear whether the device is really being installed and managed in a by a truly “shared facility”.
- Commonly, this trips up the “not-really-a-shared instrument” submission
- Important components:
  - Maintenance plan
  - Access/prioritization of projects
  - Staffing: expertise and experience are evaluated
    - Study sections don’t look favorably on applications for instruments managed by postdocs or junior faculty, who should be focusing on their own research
  - Training plan
  - Financial plan/cost recovery (a budget table is required)
  - Oversight (role of the PI and Advisory Committee)
  - All need to be taken very seriously

Institutional support

- Does not have to supply part of the cost of the instrument unless you are exceeding the cap
- Details of financial support mentioned in the proposal should match commitments described in the institutional letter of support, and describe support committed to the instrument, not the core in which it is installed.
- The letter must confirm that “the institution will commit to provide backup for the financial plan for five years from the installation date of the instrument or for its effective lifetime.”



microscope request. This device is an essential and important expansion of the intra-vital imaging efforts within CBI and the medical school. I want to make my support for the application quite clear. Accordingly, I will ensure that the new multiphoton facility that Simon proposes in the application is put into place and, perhaps more importantly, in case of a shortfall of funds to maintain the instrument I will make sure that all service costs, etc., are paid. This is a very important addition to a very important facility.

Other concerns #1

- Does the instrument eliminate bottle necks, and improve workflow and capabilities?
  - Can you show how it will eliminate bottle necks?
  - What features improve workflow?
  - Is the need for the improved capabilities demonstrated in the description of the supported research projects?
  - NEED NEED NEED

Other concerns #2

- Do not ever ask for more than you need or can justify, ever ever ever
  - Try not to design the system by committee
  - Do not package multiple instruments into one request
- Make sure the manufacturers quote (essential) is realistic and not inflated
  - Don’t forget that the panel might see many requests for the same device. If your quote has tons of extras you should justify why.
- Do not request service contract costs

Other concerns #3

- Who should be PI/PD?
  - The PI/PD does not need to be a major user or have an NIH-funded grant.
  - Core Directors can be PI/PD if they have significant expertise related to use of the instrument and will play a leadership role in its implementation and management.
  - However, if you choose to be PI/PD and are new to writing NIH grants, make sure to enlist an experienced faculty or administrative mentor to help with planning and grantsmanship.

Other concerns #4

What is Accessible Usage Time (AUT) and how do I calculate it?

- AUT = “The number of annual hours the instrument can be practically used for biomedical research”
- May be limited by maintenance time, building/facility access, and manager or operator availability
- Some instruments can run 24/7; others can be used only during standard work hours.
- Remember that you must relate % use of the instrument by Major/Minor users to AUT
- AUT calculations should be presented clearly in a table and be well-justified in the proposal.

Practical Suggestions

Organize your application neatly, and exactly as outlined in the PAR, using the suggested headings so that the reviewers can easily find the information they are looking for.

Make sure to read the “Scored Review Criteria” in *Section V. Application Review Information* of the PAR. This describes the elements that the reviewers are looking for.

Finally: Remember

- There is only one submission a year so it is SSSSSLLLLOOOOOWWWWWW
- There is only one review panel each year so do your best.
- The review panel is full of scientists who
  - Know exactly what you want
  - Live in the same world
  - Have written successful grants
  - Can be cynical!

Questions?

Starting Questions:

1) What role should a core director/manager play in application writing?

2) Is it important that the requested instrument be the only one of its kind available to Users?

3) How much consideration should be given to including research projects with grant end dates close to the S10 funding date?

4) How much do you have to justify the specific choice (both make and model) of the instrument?

5) How do you convincingly demonstrate adequate institutional support?

6) Should I go for an HEI or just apply for a regular S10 and get the school to pay the rest?

7) How much research funding must be in place for the research projects? Do mechanisms other than an R01 count as funding for major users?