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WHITE PAPER

Winning the Shared Instrumentation S10 Grant from the National Institutes of Health (NIH)

Strategies for success

1.0 Introduction

Scientific and medical progress and breakthroughs are often facilitated by developing and applying new technologies and cutting-edge biomedical equipment. Often, such equipment is too expensive to acquire and maintain through normal research grants (e.g., R01) from the **National Institutes of Health (NIH)**, but can be acquired through **NIH Shared Instrumentation Grants (S10)**. This white paper is a primer on how to successfully write an **NIH S10 Shared Instrumentation Grant (SIG)** application to advance discoveries at institutions with NIH-supported investigators. The SIG program encourages applications from groups of NIH-supported investigators who wish to purchase or upgrade a single high-end, specialized, commercially available instrument or an integrated instrumentation system for shared use amongst several investigators. The program supports the following types of instruments: **X-ray diffractometers, mass spectrometers, nuclear magnetic resonance (NMR) spectrometers, DNA and protein sequencers, biosensors, electron and light microscopes, cell sorters, high throughput robotic screening systems,** and **biomedical imagers**. Other instruments may be supported.

The **S10 grant** will not cover instrumentation that is often funded through an institution's research project (e.g., **Research Project Grant Program [R01]**), program project (e.g., **Research Program Project Grant [P01]**), or center grant programs (e.g., **P01**). The **S10 grant** supports the actual equipment only — it will not fund research activities to develop or improve instrumentation.

Each year, the NIH publishes three separate shared instrumentation grants, each with separate program announcements, but all with the same receipt dates (e.g., program announcements with specific receipt dates and application requirements, also called **PARs**, May 1/June 1). These are referred to as (1) the **Basic Instrumentation Grant (BIG)**, (2) the **Shared Instrumentation Grant (SIG)**, and (3) **High-End Instrument Grant (HEI)**. Often, the NIH refers to all of these grants as "**S10**". **PAR** numbers change from year to year.

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Below are links to PAR announcements for 2020–2021.

- **BIG Program** is limited to institutions that have not received S10 instrumentation funding of $250,001 or greater in any of the Federal fiscal years from 2018–2021. The **BIG Program** is limited to $25,000 to $250,000 awards. Instruments supported include **basic cell sorters, confocal microscopes, ultramicrotomes, gel imagers**, or **computer systems**. PAR-21-125

- **SIG Program** provides between $50,000 and $600,000 per grant. When combined with institutional support, SIG can enable the purchase of powerful equipment. PAR 21-127

- **HEI Grant Program** is limited to instruments between $600,001 and $2 million per grant. HEI would support purchase of a Thermo Scientific™ Cryo-Electron Microscope. PAR 21-126

These three S10 awards are for one year only. That is, they do not have multiple receipt dates each year. Investigators can request a single, commercially available instrument or integrated system that costs at least $25,000 (BIG Grant) but the maximum instrument funding amount for the HEI Grant is $2,000,000. For the HEI grant, even if an instrument's cost exceeds the maximum amount, the award is capped at $2,000,000.

All three instrumentation grants are sponsored by **NIH's Division of Program Coordination, Planning and Strategic Initiatives**, **Office of Research Infrastructure Programs (ORIP)** and the **National Institute of General Medical Sciences (NIGMS)**. ORIP is dedicated to supporting infrastructure in research organizations while the **NIGMS** is one of the 27 **NIH Institutes** that supports basic research such as studying the foundations for disease diagnosis, treatment and prevention. Importantly, the **NIGMS** supports research projects that examine specific clinical areas that affect multiple organ systems. In parallel, the **NIGMS** is especially interested in promoting participation in the **Institutional Development Award (IDeA)** program, which allows co-funding for applications from institutions in **IDeA** states that historically have had low levels of **NIH** funding. Thus, if the applicant's institution is located in one of these 24 **IDeA** states shown below in Figure 1 (blue on the USA map), co-funding for the S10 grant by NIGMS may be more favorable. Also, if the applicant's research aligns with NIGMS mission, as outlined above, this also could be beneficial for the application.
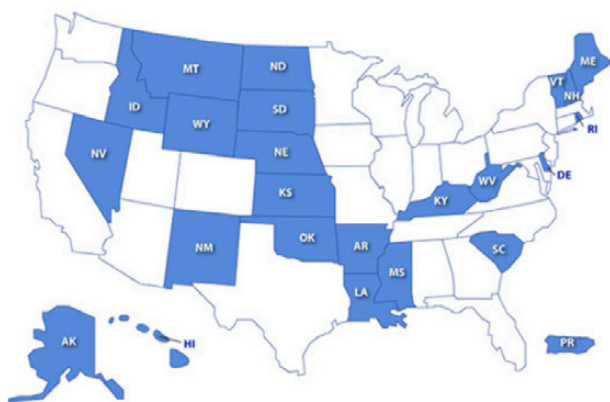

Figure 1. States included in the NIH IDeA program.

In fiscal year 2021-2022, the NIH's ORIP and NIGMS intends to commit ~$30 million for S10 grant programs. This level of funding has decreased by 45% since 2012, when $68 million was committed for S10 grants as shown in **Figure 2**, increasing the competition for shared instrumentation grants. However, the success rate of S10 grant applications is 18%-20% (the number of grants accepted versus those submitted), which is historically higher than other NIH grants like R01s. However, the award requirements are strict and applicants need to follow all guidelines and show a convincing need for the instrument in their research. There are strategies to make an application stand out, but first, applicants need to pass the eligibility requirents.
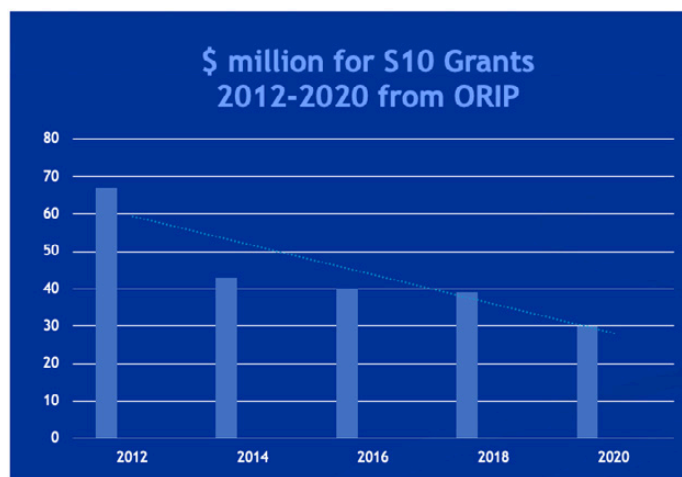

Figure 2. NIH's ORIP funding levels from 2012 to 2020.

2.0 Eligibility requirements

Unlike broad-based research grants from the **NIH**, the **S10 grant** has strict eligibility requirements and exclusions. The funding mechanism will support only certain types of instrumentation, and the requirements for equipment use are specific.

2.1 Types of Equipment

The **S10 grant** cannot support the purchase of the following:

1. New instrumentation development

2. General purpose equipment

3. Purely instructional equipment

4. Instruments used for clinical (billable) care

5. A single instrument with a base cost of less than $100,000

6. Multiple instruments bundled together to meet the $100,000 minimum

7. A series of complementary related instruments that share a common research focus

8. An assortment of instruments to furnish a research facility

9. Software, unless it's integral to the operation of a piece of equipment

10. Institutional administrative management systems

11. Clinical management systems

12. Equipment for routine sustaining infrastructure, including standard computer networks, autoclaves, hoods and equipment to upgrade animal facilities.

The supported types of instruments for S10 grants are broad based, for biomedical research, and include, but are not limited to, biomedical imagers, high-throughput robotic screening systems, X-ray diffractometers, mass spectrometers, nuclear magnetic resonance (NMR) spectrometers, DNA and protein sequencers, biosensors, electron and light microscopes, and cell sorters. The NIH provides a list of all the instrumentation allowable for the S10 grant program in each PAR. If an instrument is not on that list, applicants should ask the Program Officer (PO) if the equipment is allowable. The PO is listed at the end of each PAR announcement.

The HEI program enables the introduction of advanced, cutting-edge technologies that provide new biomedical research capabilities. For novel technology, a risk-return trade-off is expected and allowed. Due to the novelty of the technologies and the uniqueness of their implementation, specialized and technologically savvy groups of investigators will be qualified to lead the adoption of advanced instruments for biomedical research and the development of innovative biomedical applications. Therefore, if an applicant requests a novel instrument, they should demonstrate unique technical expertise that merges multiple scientific and technological fields such as biology with physics and bioinformatics.

For integrated systems, the applicant must provide a detailed description of how the system will be put together, as well as the technical expertise of the individual(s) who will be responsible for assembling the system as well as maintaining the system. The applicant must also provide a detailed description of training for the investigators listed in the application about the use of the novel technology in advancing their research. In addition, the HEI program requires that any unique instrument or an integrated system must be developed by reliable commercial vendors and guaranteed by the manufacturer's one-year warranty.

> *Caution:*
> *If an investigator is looking to fund a "stand alone" computer system, such as a supercomputer, computer clusters and storage systems, such a system must be solely dedicated to the instrument requested and must be available for NIH-supported PI research needs.*
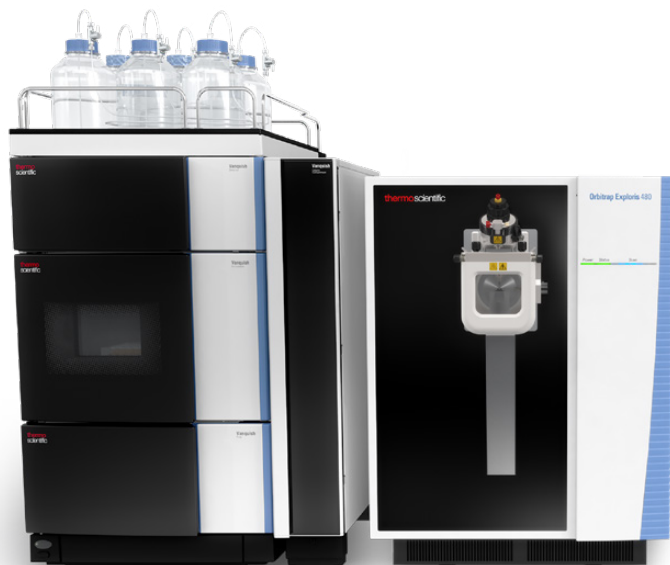
2.2 "Clinical Trial Not Allowed"

S10 instrumentation grants are all marked "Clinical Trial Not Allowed," meaning they do not directly fund research activities/clinical trials; hence, they are not subject to the NIH reporting requirements for clinical trials. A request for an instrument must be justified by the needs of active NIH-funded research projects but not include clinical trials. It is permitted for a funded instrument to be used when conducting NIH-funded human subject research, but not to be used in a trial specifically or for patient diagnostic purposes (MRI, PET). All instruments and integrated systems must be dedicated to biomedical research only.

2.3 Instrumentation is Shared and Investigators are NIH Funded

The instrument in an S10 grant will need to be shared among several investigators who are supported by NIH grants. In the grant application, applicants must identify investigators who will use the requested instrumentation under two categories: "Major Users" and "Minor Users." Specifically, at least 3 Major Users must be identified who have active NIH grants of the following type, as shown in Table 1 on the following page. Other major users can be added but need not have these grants, and 5-8 Major Users are ideal. More (e.g., 10) are not.

> *Strategy:*
> *The grant awards for Major Users should be active throughout the S10 award period, but longer funding periods beyond the S10 award is better. Also, PIs with multiple NIH grants are particularly impressive to reviewers.*

Minor Users do not fit the major user definition. They may have funding, but not have NIH research grants, or they may be new investigators without funding. Minor Users can be funded by non-NIH sources like private foundations, the US Department of Defense (DOD), National Science Foundation (NSF), NIH career awards (K), Training Grants (T32), Fellowship Awards, and Small Business or Technology Transfer (SBIR/STTR) Grants from NIH. Including such early investigators is helpful to the S10 proposal. Investigators should highlight these supplemental users to show that the its impact will benefit more than just the listed Major Users, providing a larger dynamic impact. Including Minor Users in a grant application shows reviewers the wider range of research that requires the instrument and that early-stage and new PIs will be trained on the new instrument.

> *Strategy:*
> *Promote preference of the instrument to Major Users. All NIH research projects should account for at least 75% of instrument time.*

Code	Title	Description
DP1	NIH Director's Pioneer Award (NDPA)	To support individuals who have the potential to make extraordinary con- tributions to medical research. The NIH Director's Pioneer Award is not renewable.
DP2	NIH Director's New Innovator Awards	To support highly innovative research projects by new investigators in all areas of biomedical and behavioral research.
PO1	Research Program Projects	For the support of a broadly based, multidisciplinary, often long-term research program which has a specific major objective or a basic theme. A program project generally involves the organized efforts of relatively large groups, members of which are conducting research projects designed to elucidate the various aspects or components of this objective. The grant can provide support for certain basic resources used by these groups in the program. A program project is directed toward a range of problems having a central research focus, in contrast to the usually narrower thrust of thetraditional research project. Each project supported through this mechanism should contribute or be directly related to the common theme of the total research effort. These scientifically meritorious projects should demonstrate an essential element of unity and interdependence.
RO1	Research Project	To support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing his specific interest and competencies.
R35	National Institutes of Health Outstanding Investigator	Activity code R35 is listed as 'Inactive' but was used to provide long-term grant support to investigators whose research competence and productivity are distinctly superior and who are highly likely to continue to perform in an outstanding manner.
R37	Method to Extend Research in Time (MERIT) Award	To provide long-term grant support to investigators whose research com- petence and productivity are distinctly superior and who are highly likely to continue to perform in an outstanding manner. Investigators may not apply for a MERIT award. Program staff and/or members of the cognizant National Advisory Council/Board will identify candidates for the MERIT award during the course of review of competing research grant applications in accordance with regular PHS requirements.
UO1	Research Project— Cooperative Agreements	To support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing his specific interest and competencies.

Table 1. Types of grants required for major users

Major Users can be:

- Individual researchers
- A group of investigators within the same department
- Investigator groups from several departments at the applicant institution
- NIH extramural awardees from other nearby institutions

Tip:
Pls with T, K, F, or SBIR/STTR cannot be Major Users and all must demonstrate a significant need for the instrument in their NIH-funded research.

2.4 Institution Requirements

Eligible organizations include:

Higher education institutions
- Public/state controlled institutions of higher education

- Private institutions of higher education

In particular, the following types of higher education institutions are always encouraged to apply for **NIH** support as public or private institutions of higher education:

- Hispanic-serving institutions

- Historically Black colleges and universities

- Tribally controlled colleges and universities

- Alaska Native and Native Hawaiian serving institutions

- Asian American Native American Pacific Islander serving institutions

Nonprofits other than institutions of higher education
- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)

- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

Federal governments
- U.S. Territory or Possession

Foreign institutions
- Non-domestic (non-U.S.) Entities (Foreign Institutions) are **not** eligible to apply.

- Non-domestic (non-U.S.) components of U.S. organizations are **not** eligible to apply.

- Foreign components, as defined in the *NIH Grants Policy Statement*, are **not** eligible to apply.

2.5 Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) [PD(s)/PI(s)] is invited to work with their organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for **NIH** support.

The **PD/PI** should document (in the biographical sketch) technical expertise directly related to the type of the requested instrument. The **PD/PI** does not need to have an **NIH research grant** or any other research support but is expected to be an expert on the requested instrument. The **PD/PI** may be a core director, a tenured, or a non-tenured faculty member of the applicant organization. The **PD/PI** must be affiliated with the applicant organization and registered on **eRA Commons**.

> **Warning:**
> Multiple PIs/PDs are **not allowed** *under the S10 program—only one PI/PD allowed.*

2.6 Number of S10 Applications Allowed

Applicant organizations may submit more than one application, provided that each application is scientifically distinct. The **NIH** will not accept duplicate or highly overlapping applications under review at the same time. This means that the **NIH** will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.

- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.

- An application that has substantial overlap with another application pending appeal of initial peer review.

There is no restriction on the number of applications an institution can submit to the **SIG** and the **HEI Programs** each year, provided the applications request different types of equipment. However, only one application to the **BIG Program** is allowed per receipt date. Concurrent **SIG**, **HEI**, or **BIG** applications for the same instrument or the same type of instrument with added special accessories (for example, to meet the **HEI** budget requirement), are not allowed unless documentation from a high-level institutional official is provided, clarifying that this is not an unintended duplication, but part of a campus-wide instrumentation plan. Applicants are advised to discuss any potential duplications with the **Scientific/Research Contact** (listed at the end of each **PAR**) before submitting two applications for the same type of instrument.

> **Warning:**
> *A single application requesting more than one type of instrument (for example, a mass spectrometer and a confocal microscope)* **is not appropriate** *and will not be considered.*

2.7 Special circumstances for PIs

- **If applicants have no instrumentation or no expertise:** Demonstrate that applicants and other major users have taken courses through the manufacturer and third parties on how to use the instrumentation. In addition, applicants must show that they have performed a demonstration of the equipment, generating some preliminary data on one or more research projects related to the proposal. Finally, enlist experienced users of the equipment to serve on the advisory committee.

- **If the applicant's organization has similar instrumentation**: Thoroughly describe why the other instrumentation is not accessible. For example, show how the existing instrumentation is at or slightly over its usage capacity (75% to 85%). Provide documentation of the usage with graphs and evidence from the researchers who are using this equipment.

- **If an applicant is asking for novel and new instrumentation:** Reviewers are often hesitant of funding novel/new instrumentation with few proven results or in-the-field testing. Applicants must show they have used this equipment and generated preliminary data. Applicants must also show that they have had thorough training on how to use the new equipment effectively for the applicants' specific purposes.

3.0 S10 Grant Proposal Requirements

3.1 Application contents

For an **S10 grant**, there are specified page limits for each section of the **Instrumentation Plan**. All tables, graphs, figures, diagrams, and charts must be included within the page limits. The applicants should make every effort to be succinct. It is expected that the length of the **Instrumentation Plan's** narrative depends on the type of the requested instrument and the number of users. To be successful, an application does not have to reach the specified page limits:

- Introduction to Resubmission (if applicable): *3 pages*

- Justification of Need: *9 pages*

- Technical Expertise: *3 pages*

- Research Projects: ≤ *30 pages*.
  This section can be structured in subsections **Research Projects of Major Users** and **Research Projects of Minor Users** or subsections **Specific Research Topics**.

- Summary Tables: *6 pages*

- Administration (Organizational/Management Plan): *6 pages*

- Institutional Commitment: *3 pages*

- Overall Benefit: *3 pages*

Letters of Support and **Bibliography & References Cited** sections are not included in these page limitations. Each of these sections are detailed below.

> ***Please refer to Section IV of the RFA announcement for all details and information for how to prepare an S10 application.***

The following are basic instructions on how to prepare these sections of the S10 grant.

3.2 Introduction to Resubmission (if applicable): *3 pages*

Only include this section for resubmission (A1). This section will contain responses to reviewers' critiques and what applicants have changed in the resubmission from the original submission (A0).

3.3 Justification of Need: *9 pages*

In this section, applicants should justify the need for the instrument and any necessary accessories or software used in generating results/data. All software supported by this program must be integrated in the operation of the instrument or be necessary for generation of high-quality output data from the instrument. Depending on the needs of research projects, different configurations of such software may be needed to ensure productive scientific use of the instrument.

If such additional software modules are requested (e.g., software configuration for the acquisition of metabolomics data, microscope image acquisition, control modules, or tools for MRI scanner functionalities), they must be essential for the advancement of research projects of least **3 Major Users**.

Detail the scope of the proposal with the user groups, instrument, cost, and instrument capabilities.

1. History of the core facility where the instrument will be housed. Explain where the shared facility is located in the institution.

2. Describe instrument and historical perspective about the development and evolution of the instrument and technology. Applicants must clearly demonstrate they understand the technology and appreciate the pros and cons of the instrument's application.

3. Rationale for selecting instrument and importance to the research objectives.

4. Compare requested instrument with other similar, commercially available.

5. Describe access to existing equipment and why it is either unavailable or unsuitable.

6. Provide a summary of the proximal inventory of similar systems that might have been used but cannot be for one reason or another.

In this section, *include letters* from the owners or core directors of the other instruments that attest to the reason these instruments are unavailable.

3.4 Technical Expertise: *3 pages*

In this section the applicant must convince the reviewers they have the technical expertise to set up and run the instrument requested. Include the following information:

1. Describe the technical expertise of individuals who will set up and run the instrument. Discuss the **technical/scientific advisory committee** the applicant has established. List **advisors** and **consultants** who will advise on experimental design, use, and application of the instrument.

2. Specify who will ensure that the instrument is safely operated and appropriately maintained. Detail **biosafety/biohazard** protocol.

3. State who will **train new users**.

4. If the instrument requires complex sample preparation or consultation for experimental designs, describe the **experts** who will serve in that capacity.

5. Address **technical support** for data collection, management, and analysis.

> *Tip:*
> *Since the research projects have been previously peer reviewed, describe their details only as necessary to explain how the requested instrument will advance the projects' research objectives.* **Do not** *copy the* **Specific Aims** *of an already funded application.*

3.5 Research Projects Section: *30 pages*

Applicants can organize this section into subsections "Research projects of Major Users" or "Specific Research Topics." This format may be especially useful to avoid redundancies in the presentation of research projects for which several Major Users pursue research topics that follow similar protocols and offer comparable scientific benefits. All Major Users must demonstrate a substantial need for the requested instrument through their NIH-funded research projects.

Present sufficient technical details about how samples or specific experimental protocols will be used, which allow reviewers to evaluate whether the instrument is appropriate, whether it will be effectively utilized, and provide advantages over other similar existing instruments. In particular, explain the need for any special features, accessories, or special software modules within the requested instrument, describing the specific studies that will use these options for at least 3 Major Users.

Although preliminary data are not required, they can illustrate the benefit of the requested instrument to the research projects. Describe how generated data will be handled and analyzed so that benefits of the entire experimental setup can be evaluated. Summarize benefits that the requested instrument will provide towards answering specific scientific questions. Be both succinct and clear.

If applicants choose to structure their Research Projects section by including the "Research Projects of Major Users" subsections, limit the text to no more than 4 pages per each Major User's project. In the beginning of each Major User's narrative, list the PI's name and grant information.

> *Tip:*
> *Focus the research projects section on detailed explanation of how the requested instrument will advance funded research projects. Applicants **must** show a significant need for the instrument in NIH-funded research.*

For certain technologies such as computer systems or X-ray detectors, there may be a larger number of users, exceeding what is necessary to make a strong case for the need of the instrument. Remember that the number of users alone is not a compelling way to justify scientific needs for the requested instrument.

If there are Minor Users and other lesser users, include up to 4-page long section entitled "Minor Users' Projects." Describe the need for the requested instrument to advance projects from Minor Users and the user community at the institution (e.g., unfunded users who have significant need for the instrument to develop their research programs or users whose expected needs are at the level of 1% or less of the expected usage time). Include a sum of the anticipated usage in annual hours for all minor or other users.

Each research project should be organized as:

1. PI name and title, PI role, and project title

2. Specific aims

3. Background and significance

4. Preliminary results that validate the need, use, and application of the requested equipment. Ideally, the data will be gathered on the requested instrument.

5. Experimental procedures and protocols. Provide sufficient detail to demonstrate an understanding of the use of the instrument and of difficulties that may be encountered.

6. Use, application, and need for the requested instrument in fulfilling specific aims. Address specific accessories requested and the unique instrument capabilities.

3.6 Summary Table(s): *6 pages*

Summary tables must include "Table 1: Research Projects of Major Users" and "Table 2: Research Projects of Minor Users." These two tables should be formatted like the following example, for each user:

User Name	Grant No.	Brief Title	Grant start/end	Est. Usage (Annual Hrs)
Jenkins, JA	3 R01 CA139393 09	Structural Refinement for Macromolecular Structure by NMR of Immune Proteins	Nov 2019/ Jan 2022	168 hours

If there are multiple users funded by the same grant, list a total of their estimated usage in annual hours for projects supported by that grant. If applicable, include a separate table to indicate the users' needs for any requested accessory. If a special use instrument (SUI) is requested, these tables should clarify accessories which are not needed for the Major Users or the Minor Users. Do not list users whose annual usage is at the level of 1% or less of accessible user time (AUT).

3.7 Administration (Organizational/Management Plan): *6 pages*

The investigator applying for an S10 must convince the study panel that the instrument will be well utilized and cared for during its useful service life. This section is intended to show that and should contain the following:

1. Describe the entity or core facility that will oversee the instrument—list names and titles of the members of the local advisory committee. The membership of the Advisory Committee should be broad to balance interests of different users and should include members without conflicts of interest (non-users of the requested instrument) who can resolve disputes if they arise. The membership of this committee should include at least one senior institutional official who will represent the financial commitment of the institution. It is recommended that the Advisory Committee includes at least 4 members. Major and other active users (such as Minor Users) of the instrument may be members, but none should be the Chair. The PD/PI cannot be a voting member of the Advisory Committee. The PD/PI and the

Advisory Committee should convene meetings and prepare annual reports on the instrument status. The reports will become part of the Final Research Performance Progress Report (Final RPPR) and the Annual Usage Reports (AUR).

2. Describe location and space where the instrument will reside, including architectural and engineering drawings as needed and any necessary renovations.

3. Discuss administration of the instrument including the oversight advisory committee that oversees instrument access, scheduling, and dispute resolution.

4. Detail role and composition of the technical advisory committee.

5. Provide an operating budget table covering the first four years that includes anticipated expenditures for staff, supplies for the instrument, usage hours, and anticipated recharge income.

6. Describe a plan for managing access to the instrument if users' projects involve human subjects, vertebrate animals, or biohazards, such as infectious materials

3.8 Institutional Commitment: *3 pages*

Applicants must show that their institution is willing to support the equipment that they wish to purchase using a combination of several methods. First, show prior competence and support of the core facility to demonstrate historical trends of instrument use, training, maintenance. Applicants must show their institution is willing to dedicate and renovate dedicated space for the equipment. Staffing support, service contracts, and letters from senior administration officials (Chair or Dean) are required to show support in perpetuity for the instrument.

Warning:
Don't skimp on Letters of Support to show institutional commitment.

Also, define the institutional costs to the organization for running and maintaining the equipment. A specific statement from the institution that they will support the service contract for this instrument for the next five years (e.g., warranty plus four years' contract) provides a firmer commitment, especially with new equipment. Get specific dollar amounts whenever possible.

One outstanding method of demonstrating institutional commitment is to show that applicants have already planned a website describing the shared facility to the research community (at their institution and those outside). Even though applicants don't have the instrument yet, they can show a mock-up of such a page, a common practice with many PIs. Examples from two institutions are shown in Figures 3 and 4. Such websites demonstrate that applicants have planned on the shared facility inclusion of their instrument.

Figure 4. MIT shared facility website showing the Thermo Scientific Talos™ Artica™ G2 Cryo-EM Instrument

Figure 3. Weill Cornell Medicine website showing Microscopsy and Image Analysis Core Facility (left) and the Microscopy Offerings page (right) that describe equipment, its use, and how to reserve the equipment.

3.9 Overall Benefit: *3 pages*

Succinctly convey the broad benefit of the new instrument to the greater research community. Applicants should convey how the instrument will impact **NIH-funded** research and contribute to the institution's long-term biomedical research goals.

Place the instrument in the context of the **core facility** and communicate the instrument's broad benefit to the core facility and to the **research infrastructure** of the university. Essentially, the applicant should describe how will this instrument benefit **Major Users** and **Minor Users** and move the field forward, i.e., what will its overall impact be to the applicant's research group and the wider research community?

> ### Strategy:
> Convey **strongly** the impact this instrument will have overall—that is, the likelihood (probability) this instrument will exert a sustained, powerful influence on the institution's long-range research goals and specifically move forward the research of the **NIH-funded Major Users**.

3.10 Letters of Support

Letters of Support should include not only the letters from institutional officials professing institutional commitment, but also letters from biosafety committee if necessary. All letters of support should be combined into a single file named Letters of Support and uploaded as a separate attachment via Other Attachments. This combined file should include:

- **Letters** from institutional officials.

- **Institutional back-up** for the proposed financial plan.

- Letters about **inventory of instruments** at the institution which are unavailable to the **PD/PI** (as noted in the *Justification of Need Section*), as applicable.

- The institution (i.e., the **entity with the same DUNS number** as the applicant's institution) must also provide a table that includes information about performance of all previous **S10-awarded instruments** within the past five years. If there have been no awards, please state that. The table should have the following **9 columns**:

   1. S10 Grant Number
   2. Year of Award
   3. Installation Date of the Instrument
   4. PD/PI's name
   5. Generic Name of Instrument
   6. Instrument Status: *Active* (instrument in use), *Pending* (order placed, but instrument not delivered, instrument received but not installed or not calibrated for general use), *Upgraded* (or *Replaced*), *Not Available* (sold, decommissioned, transferred) — If the instrument is currently **non-functional**, provide a succinct explanation of the instrument status immediately following this table
   7. **Actual Usage Time:** Actual total time in **hours per year** the instrument was used for research. if the instrument has been functioning for less than a year, the usage time can be extrapolated to annual hours

   8. Maintenance Agreement: Active (Warranty in place), In-House (or Self-Insured), None (Fee for Service, Pending), Not Available (no longer supported by manufacturer)
   9. Publications: Enter the number of research publications that cite the S10 award or have been linked with the **S10 award** in My NCBI. The number of reported publications should be verified in the **NIH RePORTER**. If there are no publications for any of the previously awarded **S10 instruments**, provide an explanation immediately following this table.

- Letter from **Biosafety Official**. If **human, animal**, or **infectious materials**, which could create a potential **biohazard**, are to be analyzed, a signed letter is required from the institutional biosafety officer stating that the proposed containment plan has been reviewed and adheres to documented **biosafety regulations**. If relevant, this letter is required in the application.

3.11 Other Project Information

Project Summary/Abstract

This should contain a succinct and accurate description of the requested instrument and an explanation of the need for the instrument to advance research projects of the users. The application's broad, long-term objectives should be stated, concisely describing how access to the instrument will enhance the health-related goals of the research projects. This section should be informative to other persons working in the same or related fields and understandable to a scientifically or technically literate reader. This section must be no longer than 30 lines of text.

Project Narrative

Using no more than two or three sentences, describe the relevance of this research to public health. In this section, be succinct and use plain language that can be understood by a general, lay audience.

Bibliography & References

Cited List only publications that demonstrate the researchers' expertise in operation and usage of the requested instrument or that are relevant to research projects, which will be supported by the instrument. References of the Research Projects section may appear here or may be listed at the end of individual research subsections.

Equipment

Describe the requested instrument by stating its manufacturer, model number, specific features, and accessories. Provide a detailed budget breakdown of the main instrument and requested accessories, including tax and import duties, if applicable. An itemized quote from the vendor, with appropriate discounts and warranty terms, is required. The quote must be scanned and combined in a single attachment with the equipment description as part of this upload. Include an explanation of Total Non-Federal Funds in this section (if applicable). Applications without a quote will be deemed incomplete and will be returned to applicants without review.

If human, animal, or infectious materials, which could create a potential biohazard, are to be analyzed, funds for accessory containment equipment for the instrument may be requested in the budget.

4.0 Strategies for Writing the S10 Grant

Applicants can employ a few strategies in writing their application. Some costly mistakes can make or break an applicant's chance at S10 funding.

4.1 Mistakes to avoid

There are certain mistakes that the applicant can make in the S10 grant application that will trigger a rejection of a proposal, sometimes without any review:

No itemized quote(s)

Not providing itemized vendor quote(s) is perhaps the biggest mistake applicants make in their S10 application. Applications that do not include quotes will not be reviewed. The itemized quotes should accompany a detailed budget breakdown of the instrumentation and accessories, including tax and any import duties. Applicants must scan the vendor quote and include it in a single attachment with the equipment description.

Copying vendor descriptions.

Describe the requested equipment specifically and do not just copy the vendor descriptions. Include the manufacturer's information, the model and all the descriptive details of each component or accessory that is being requested. If applicants are vague about the equipment they are requesting, reviewers are not likely to move the application forward.

Neglecting biosafety

Identify and address any biohazards associated with using the requested instrumentation. Applicants must also include a letter from their institution's biosafety officer or committee.

Requesting nonessential accessories

Applicants should be aware that although some of their instrument users might lobby for certain components or accessories, that doesn't mean they should be included in the application. Applicants need to make sure that any quoted instrument components are actually needed by at least half of the users. Requesting non-essential accessories can stop the application from moving forward.

Skimping on descriptions of Major Users

Make descriptions of Major Users clear and complete by highlighting the expertise of the Major Users in the requested instrument as well as how the new instrument will enhance their research.

4.2 Follow Expert Tips

Some tips may appear more obvious than others. Yet some strategies will not just ensure that the application will make it to a reviewer's hands, but further ensure that the proposal will rise above the others. Heed these tips:

- Justify all accessories. Applicants must not only describe any requested accessories or components, but also specify which investigators need each component. At least half of the users should have a justified need for each accessory.

- Present a strong Management Plan. Sound financial planning and solid technical expertise can help applicants build a strong management plan. Having a thorough plan for training and recruiting new users is also essential. Reviewers need to see that applicants have thought ahead and planned well for maximizing usage of the requested instrumentation.

- Include a Data Management Plan. Although it's not required, if the applicant wants to impress reviewers, include a Data Management Plan in the *Organizational/ Management Plan*. This will demonstrate that the applicant is thinking ahead and prepared for the instrument's success. Many instruments allowable for the S10 grant generate a significant amount of new data and therefore a cohesive plan to manage the data is a positive aspect in the application. It is not required, but such a plan shows that applicants have thought not only how to acquire the instrument, but also what will be done with the information that comes from it. For example, will the data be archived? How will applicants ensure that investigators have access to the data?

- Focus on institutional support

- Reviewers tend to place emphasis on Institutional Commitment. They want to know that an institution is committed to supporting the instrument's upkeep well beyond the award period. Institutional support is critical success, and the applicant's institution must be receptive and supportive of the new instrument.

- Tout training and outreach.

Long-term instrument support means new users will be brought in. Getting the most out of a new instrument demands robust training. Applicants should detail how they will recruit new users and existing users through planned lecture series, online training, technical support, and consultation.

4.3 S10 Grant Example

The Office of Research Infrastructure Programs (ORIP) maintains a listing of shared and high-end instrumentation awards, the abstracts of which are available on the NIH RePorter website https://orip.nih.gov/construction-and-instruments/s10-instrumentation-programs/filterable-awards-table. Below is a listing of 2019 S10 grant awards and one award for $2,000,000 for a Talos Artica G2 electron microscope.

Year	Grant Number	PI Name	Title	Instrument Type	Institution	State	Award ($)
2019	S10OD026926	Dorit Hanein	CMOS Imaging Device for the T12 at SBP	EM	Sanford Burnham Prebys. Medical Discovery Inst.	CA	$207,306
2019	S10OD026881	Adam Frost	Glacios™ Cryo Transmission Electron Microscope with 200 kV XFEG optics	EM	Univ. of California San Francisco	CA	$1,845,637
2019	S10OD026871	Nathan Gianneschi	K2 Camera for Soft Matter Transmission Electron Microscopy	EM	Northwestern Univ.	IL	$662,750
2019	S10OD026776	Sara Miller	Transmission Electron Microscope (TEM)	EM	Duke Univ.	NC	$599,900
2019	S10OD026790	Andrew Dudley	Apreo VS-QUO-82252-P9W1 R1	EM	Univ. of Nebraska Medical Center	NE	$651,469
2019	S10OD026989	Timothy Bromage	Field Emission Scanning Electron Microscope	EM	New York Univ.	NY	$581,107
2019	S10OD026822	Susan Hafenstein	Talos Artica G2	EM	Pennsylvania State Univ.-Univ. Park	PA	$2,000,000

The above S10 grant from Pennsylvania State University was successful because it clearly showed the need for the Talos Artica G2 and detailed the groups of investigators and projects that would be significantly impacted by the use of the instrument. Each of the user groups were clearly listed and the submission showed the significant need for the instrument to conduct research that had already been funded by the NIH.

On the following page is the abstract and narrative (Public Health relevance statement) from this grant with reasons it was successful.

S10 Abstract Funded by NIH	Comment

Abstract

The specific Cryo-Electron Microscope (cryo EM) to be acquired is an **FEI Talos Arctica** that is a 200 kV Transmission Electron Microscope (TEM), with a Falcon 3EC direct electron detector, and a 12 position autoloader (AL). We are seeking to acquire the Arctica for vitrification-screening of samples to queue for data collection on the one year-old Titan Krios, which is fully operational although overwhelmed with samples, most of which are not ready for data collection. To obtain 3-D structures from cryoEM data, single particle reconstructions rely on collecting different two dimensional views of the same object that are then reconstructed into a 3-D map. The subjects for visualization by the users of this acquisition grant range broadly. Included are many multi-protein complexes, enzymes, DNA-protein complexes, RNA structures, and virus- receptor and virus-antibody complexes. The diversity of these projects, each chosen because of the likelihood of success showcases the powerful application of cryo-electron microscopy techniques. *We identify 6 Major Users, 3 Minor Users, and 3 other users, making a total of 12 labs*. The projects described are ready for cryo EM and absolutely depend on vitrification-screening to succeed and proceed to data collection and data processing using single-particle reconstruction approaches.

Clearly identifies the instrument and accessories.

Why the instrument is needed.

Detail on what the instrument will be used for.

How the instrument will fill needs from a wide diverse group of investigators at the institution.

Narrative: Public Health Relevance

The new Talos Arctica will bring much needed screening capabilities to Penn State, *enabling the ongoing research of our established Major and Minor Users.* A camera upgrade and other minor additions will also allow data collection for micro-electron diffraction that will add versatility to Penn State structural biology. The requested cryo-electron microscope will be *used to investigate many important aspects of viruses, proteins, protein complexes, polymerase modulation, RNA metabolism, DNA replication complex, cell wall synthesis, transcription activation, and structure-function studies of photosystem I, all of which will significantly enhance ongoing research projects funded by NIH.*

Why the instrument is relevant to overall public health and details what the instrument will be used for.

They point out the research for this instrument is already funded by the NIH, a requirement for the Major User groups

5.0 Conclusion

The NIH S10 Instrumentation Program is an ideal mechanism for Shared Facilities to acquire new technology, to replace and update aging instrumentation, or remain current as mature technologies progress. Clearly demonstrate the need scientifically and detail how the shared facility will provide infrastructure support for operation, training and maintenance to submit a successful application.

To significantly increase chances of success, follow these five steps:

1. Plan the submission in advance—at least 6-8 months (see below).

2. Assemble a solid user group with a demonstrated need for the requested instrument.

3. Demo the requested instrument to allow user groups to obtain preliminary data (this requires advance planning and teamwork).

4. Give the user group an early deadline to submit their project descriptions.

5. Recruit at least three NIH-funded investigators to form a user group. Of the Major Users, at least 75% should be funded by the NIH or other federal agencies such as the National Science Foundation (NSF), the Department of Energy (DoE), or the Department of Defense (DoD).

Begin at least 6-8 months ahead of the June 1 submission date to prepare an S10 Grant.

A suggested timeline for preparing a successful grant is shown below:

Month before due date	Task
September-December	• Identify the technology • Identify NIH-funded Major Users • Compile a list of vendors
January-February	• Obtain Institutional approval • Prepare demo samples
February	• Demo selected instruments • Acquire quotes on instruments
March	• Select the appropriate instrument • Write technical justification • Write business plan • Collect major user NIH biosketch
April	• Review major user projects
May-June	• Review assembled application • Submit grant application

thermo scientific

In conclusion, applicants should begin by first reading the **program announcement (PARs)**. Details of grant organization and specific requirements change yearly. Be sure to observe the page limits for each section. A submission will be rejected for not following guidelines.

The applicant's job is to communicate the user group's need for the particular instrument to the study panel. Highlight the six or more major criteria weighted in scoring a shared instrumentation grant in the forward/summary:

1. Justification of need

2. Technical expertise

3. Research projects

4. Administration

5. Institutional commitment

6. Overall benefit

Refer to the **ORIP website** for additional answers to questions about these instrumentation grants:

https://orip.nih.gov/construction-and-instruments/s10-instrumentation-programs/frequently-asked-questions-shared-and-high

Finally, the **NIH** encourages email and direct calls from **PIs** about these grants. **Research Contacts** are:

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Find out more at **thermofisher.com/EMFunding**

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