OMB Number: 4040-0001
Expiration Date: 11/30/2025

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ○ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ○ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ○ **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Project_Summary_2023_FINAL.pdf
8. Project Narrative*	Narrative_2023_FINAL.pdf
9. Bibliography & References Cited	Literature_Cited_2023_FINAL.pdf
10.Facilities & Other Resources	
11.Equipment	
12. Other Attachments	Overview.pdf Scientific_Justification_and_Facility_Development.pdf Annotated_map_views.pdf Line_drawings.pdf Dimension_Table.pdf Equipment_Table.pdf Active_grants.pdf Project_timelines.pdf Budget_Justification_and_Quotes.pdf Institutional_Support_Letter.pdf Certification_of_Title_to_Site.PDF Support_Letters.pdf

PROJECT SUMMARY

The Oregon State University Sinnhuber Aquatic Research Laboratory (SARL) is seeking funds to modernize an integrated specific pathogen-free zebrafish core facility. Our NIH biomedical research base has grown exponentially over the past decade and renovation, and modernization will ensure that it remains a critical resource to support research growth for well-established NIH Centers, individual NIH-supported investigators, and other stakeholder partners. The SARL supports Oregon State University's thematic research areas: the science of sustainable earth ecosystems, health and wellness, and economic prosperity and social progress. Completion of this project will provide modern, sustainable, specific pathogen-free zebrafish housing space, specialty research space, and efficient fish life support and husbandry systems. Our overarching goals are to 1) Renovate an existing 3,500 ft^2 purpose-built aquatic facility into a highly researcher-accessible zebrafish housing facility, 2) Replace obsolete and undersized zebrafish life support system, 3) Install modern zebrafish housing enhanced by automated cleaning, feeding, and remote monitoring, 4) Build specialty zebrafish rooms to support short and long term flow-through studies, 5) Add high capacity tank washing capabilities, and 6) Provide engineering space to further seed technological innovations. This renovation will be part of an existing research building with 10,000 ft^2 of renovated space that houses a fully automated zebrafish high throughput chemical screening facility, modern imaging and molecular biology rooms, a 2,300 ft^2 room for zebrafish behavioral studies, dedicated quarantine rooms, walk-in cold storage rooms, high-speed fiber-optic data transmission, large researcher office spaces, and modern meeting rooms. A key design principle for the SARL is that it seeds multidisciplinary interactions by providing a full menu of services. The SARL nucleates research programs through aggressive promotion of the zebrafish model. Completing this modernization project will address bottlenecks limiting further growth of zebrafish biomedical research. This proposal is part of the long-term commitment to developing and maintaining advanced aquatic biomedical research facilities at Oregon State University, the region, and nationally.

NARRATIVE

The SARL has supported NIH researchers for over fifty years by adapting to current and future researcher needs. OSU leadership recognizes the importance of this facility to achieve campus strategic goals in the science of sustainability health and wellness, and economic prosperity and social progress. With the exponential growth in the campus zebrafish NIH biomedical research base over the past decade, accomplishing the deliberate SARL renovation and modernization will serve as a critical resource to support biomedical research for another fifty years and beyond.

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OVERVIEW

The Oregon State University (OSU) Sinnhuber Aquatic Research Laboratory (SARL) is a multi-use core facility that is key to the Oregon State University NIH Research Enterprise (see letter of support from the Dean of Agricultural Sciences, Staci Simonich). The first module of the current SARL building was constructed in 1964, with additions in 1981, 1987, and 1989. It was originally constructed to investigate the nutrition requirements of rainbow trout and later as a translational carcinogenesis and chemoprevention research lab using rainbow trout. Among its notable past research accomplishments were the two largest ultralow dosage carcinogenesis studies ever conducted in any vertebrate species (each with ~42,000 trout maintained for a year). The SARL has been directly supported by the National Institutes of Health (NIH) for more than 59 years and currently supports researchers who received over six million of 2022 Annual Federal Direct Cost Funding (NIH funding totaling $4,601,631). In addition to the current 11 NIH-funded grants, two multi-investigator NIH Centers and dozens of academic, federal, and commercial entities depend on SARL-provided services. The 17,000 sq. ft. SARL laboratory is directed by Dr. Robyn Tanguay (since 2003) and is supported by the College of Agricultural Sciences, the OSU Office of Research, and a robust fee-for-service revenue stream utilized by dozens of academic and commercial scientists. The SARL provides capabilities found nowhere else in the world to support biomedical research using zebrafish. Zebrafish models of human biology are proven, relevant, rapid, cost-effective, and a powerful research platform for biomedical studies. In 2009, the facility moved to support exclusively zebrafish research with the long-range goal of developing the zebrafish into a premier vertebrate biomedical research model. SARL staff have achieved several milestones to place it at the forefront of zebrafish research: the first and only specific pathogen-free zebrafish facility, the first defined diet for zebrafish, a standardized outbred “wild-type” zebrafish, and multiple innovative technologies to automate breeding and zebrafish handling. For example, SARL staff invented spawning tanks to produce near-limitless precisely timed zebrafish embryos throughout the day. The Core Director was awarded an NIH Director’s RC4 grant to invent and build robots to automate the handling and exposure of at least 30,000 zebrafish embryos per day, along with custom-designed instruments to measure complex visible and behavioral phenotypes. Substantial investments in software solutions have advanced rigorous and reproducible research. The SARL manages projects and data sharing using an in-house developed laboratory information management system.

For the past decade, OSU has been aggressively remodeling the SARL in stages with institutional support, which has resulted in a heavily used, but increasingly inefficient facility. Although the automation, molecular biology, chemical handling, behavioral assessment, and researcher office spaces are now state-of-the-art, the animal housing spaces, zebrafish life support systems, researcher accessibility, and energy efficiency are functionally obsolete and are measurably hampering researcher access and productivity. Completion of this proposal would address each of these challenges. We specifically propose to:

- Renovate the existing currently unused 3,500 sq. ft. North Wing of the SARL facility by replacing the roof, installing a ceiling, adding floor drains, installing flooring systems, improving insulation, improving workflow and disability access.
- Add efficient HVAC systems for renovated space (unused wing not currently temperature controlled)
- Replace all existing obsolete life support and rack systems as they are failing
- Build a modern efficient zebrafish tank room with 18 racks that meets AALAC standards
- Create space for mass spawning and specialized genotyping racks to accelerate screening
- Construct two zebrafish tank rooms for specialized short and long term experiments
- Construct a flexible prep room for microinjections, genotyping and tissue collections
- Install fish feeding robots to reduce labor cost and to decrease generation times
- Modernize and increase the efficiency of fish tank-washing
- Renovate engineering space to further enable innovation in research instrument development

PROJECT NARRATIVE

Scientific Justification

The SARL is a full-service facility with a mission to help investigators leverage the unique advantages of zebrafish (1, 2) as they focus on understanding the environmental-biological interactions that influence human disease. The SARL gives investigators access to the full range of services and resources (3). The SARL brings investigators the powerful zebrafish research platform (4, 5), a hatchery for rearing specific pathogen-free zebrafish (6), and a unique biomedical research facility for high-throughput studies of nutrition (7-9), genetics (10, 11), and toxicity (4, 12). SARL staff consult with investigators to establish the suitability of zebrafish for their translational studies, then helps them design and execute those studies. Staff expose zebrafish embryos to chemicals in accordance with well-established protocols (4) and then help investigators acquire their data. SARL staff provide *a*) technical support, including tank allocations, feeding, and specialized diets, *b*) expertise in surgery, microinjection, necropsy, histopathological evaluation, and imaging (13), *c*) support for broad-based "omics" experiments linked to adverse outcomes (14-17), *d*) expertise and advanced equipment for developmental-, juvenile-, and adult-stage zebrafish neurobehavioral studies (18, 19), *e*) transgenic and zebrafish mutant line production(20), f) support for compliance issues, and g) collaboration with investigators to interpret and statistically analyze data.

Focused on Innovation and Impact of Recent Infrastructure Improvements

The SARL employs a team of engineers and staff scientists who evolve and innovate our capabilities to meet researcher needs. Below is a partial list of recent improvements:

- Created the World's First Specific Pathogen-Free (SPF) Zebrafish Facility
- Developed Robots for Automated Embryo Handling
- Developed Instruments to Remove Embryo Chorions
- Developed Efficient Large-Scale Embryo Production Systems
- Created Specialized and Defined Zebrafish Diets
- Developed Hardware that Sorts Zebrafish Embryos

Figure 1. Existing facility with automated instrumentation

- Created Machine Learning Software that Counts Zebrafish Embryos and Objects
- Created Instrumentation for Early life and Adult-Stage Zebrafish Behavioral Assessments
- Integrated Custom and Commercial Instrumentation into a High-Throughput Bioactivity Screening Pipeline
- Built a new Platform to Assess Respiratory Fitness of Adult Zebrafish
- Developed a Complete Digital Curation Platform for Multidimensional Data Management and Analysis
- Modernized ~2300 ft² of the existing facility for Behavioral studies

Because of the unique services offered, the SARL supports a diversity of NIH-funded researchers (**summarized in Table 1 below, letters of support, and attachment 4**). Additionally, the core supports important federal and other stakeholder-driven research. A few selected examples below illustrate how SARL researchers apply unique resources to support investigator-driven and stakeholder-driven biomedical research.

Impacts of Zebrafish Disease on Research. Dr. Michael Kent was instrumental in establishing the SARL as an SPF facility and is now studying the common zebrafish pathogens. He has worked with the SARL to demonstrate that the control of pathogens is critical for colony health and for improving research reproducibility (21, 22). He currently focuses on the development of methods to control and avoid these pathogens (R24 OD010998). The SPF fish provided by the SARL are essential. This modernization project will allow Dr. Kent and SARL staff to provide a new service to the zebrafish community to re-derive valuable zebrafish mutant and transgenic lines into SPF backgrounds (see Kent letter of support). Monte Westerfield, the Director of the Zebrafish International Resource Center (ZIRC), agrees that the zebrafish community increasingly needs a source of SPF fish from this service (see Westerfield letter of support).

Predictive Toxicology. The NIEHS has established *Predictive Toxicology* as a strategic goal for advancing environmental health sciences. The overarching goal of the new prestigious and eight-year R35 grant awarded to Tanguay (R35 ES031709) "Discovering Chemical Activity Networks-Predicting Bioactivity Based on Structure" will use the SARL to expose millions of zebrafish embryos to libraries of synthetic chemicals across wide concentration ranges. They will systematically analyze gene expression changes to formulate hypotheses about which biomolecular targets the chemicals attack initially and which pathways lead to the observed phenotypes. To test those hypotheses, they will use the SARL to edit the zebrafish genome via CRISPR/Cas9. The SARL will help share experimental results in public databases and its machine-learning-based chemoinformatic tools to analyze zebrafish data and infer relationships between the structure of a chemical and its biological activity. This work will enable scientists to predict whether a chemical will be biologically active, what target it will act upon, and what networks it will perturb, solely based on its structure.

Table 1 Summary of Current SARL Users

Major Users	**43**
Academic	34
Commercial	9
SERVICES	
Distribute SPF embryos/fish	**19**
Oregon State University Users	4
Others (outside Oregon)	15
Experimental Support	**29**
Oregon State University Users	8
Other Academic Institution	12
Commercial	9

Commercial e.g., P&G, MERCK, Regeneron, Battelle, Sudoc, Ramona Optics, ICL, AsedaSciences
Academics e.g., Cornell, Yale, North Carolina State U, Washington State U, Children's Hospital- LA, UC Berkley Louisiana State U, Woods Hole, UC Riverside, University of Ottawa

Advanced Understanding of Diseases associated with Microbiome Dysbiosis. Disruption of the human microbiome can cause various diseases and increased susceptibility to environmental stressors. Dr. Thomas Sharpton developed a high-throughput infrastructure to study interactions between the zebrafish gut microbiome and dietary exposures to triclosan. His group found that the biological functions encoded in the zebrafish and human gut microbiomes are conserved along with a similar taxonomic structure. The Sharpton group found that acute triclosan exposure rapidly diminished ($p < 0.05$) the gut abundances of *Plesiomonas*, *Coprococcus*, *Rhodobacter*, *Bacteroides*, and *Ruminococcus* in treated fish (23). His group recently published an integrated gene catalog of the zebrafish gut microbiome demonstrating that it has significant homology with mammalian microbiomes (24). Dr. Sharpton received an NIEHS R01 (ES030226) aimed at understanding the role of the gut microbiome in polycyclic aromatic hydrocarbon neurobehavioral toxicity. Drs. Sharpton and Kent are also investigating Interactions between Gut Microbiome Natural Products and Intestinal Helminths using zebrafish.

Determined Biological Activity of Pre- and Post-Remediation Bioproducts. In remediated environments, Dr. Staci Simonich identified many previously unidentified nitrated polycyclic aromatic

hydrocarbons (PAHs), some of which are highly mutagenic (25). Dr. Simonich also found that mycobacteria in the environment biotransform phenanthrene (a PAH) into numerous metabolites. She assessed those metabolites in zebrafish and discovered that the oxygenated metabolites are more toxic than the parent compound. She received a grant from the Department of Defense to continue these studies (26). The current Semprini/Simonich NIEHS-funded Superfund Project aims to predict and identify PAHs in the environment and characterize their toxicity across life span using the zebrafish model.

Determine the Biological Effects of Chemical Mixtures in Complex Environments: Dr. Kim Anderson's group uses innovative passive sampling technology to measure environmental and human exposures in real-world settings to gain a better understanding of the diversity of chemicals that pose a risk to human health. In addition to her impressive analytical measurements, she uses the SARL to evaluate chemical toxicity in zebrafish (27-33). The current Anderson NIEHS-funded Superfund Project is now applying this approach to study the toxicity of other chemical mixtures. These data are vital to advance 21st-century chemical risk assessments to protect and improve human health.

Harness the AhR Pathway to Treat Immune-Mediated Diseases: Dr. Siva Kolluri is identifying AhR ligands by virtual ligand screening (VLS). He has generated a homology model of the mouse and zebrafish AhR ligand-binding domains (LBD) based on homology with other PAS proteins with known three-dimensional structures and empirically validated their activity at the SARL (34-37). He tested these compounds in cell-based experiments and identified six new AhR ligands that strongly activate AhR transcription in reporter gene assays (38). Kolluri and his colleagues use the SARL to evaluate the actions of these ligands in zebrafish to help prioritize mammalian studies. The long-term goal is to develop AhR ligands with reduced toxicity as lead compounds for human therapeutics.

Understanding Congenital Hearing Loss. Dr. Colin Johnson's research program is focused on congenital hearing loss, which is a common disorder affecting approximately 1 out of every 600 children. His lab focuses on the protein otoferlin since mutations in otoferlin explain up to 8% of all forms of prelingual autosomal recessive hearing loss (R01 DC014588). To screen for the effects of pathogenic mutations on otoferlin function, he developed truncated forms of otoferlin in zebrafish. The SARL generates and houses these zebrafish lines, supports gene expression analysis, imaging, and performs behavioral assessments with the Johnson group.

Define Epigenetic Transgenerational Toxic Effects: The SARL will continue to support researchers studying epigenetic mechanisms. As an example, B[a]P-mediated neurobehavioral defects in larval zebrafish that persist to at least the F2 generation is also associated with a 40% reduction in global DNA methylation in the F0 and reduced expression of DNA methyltransferases 3A1 and 3A2 (10). Since B[a]P toxicity requires AhR signaling, it is important to understand how AhR participates in epigenetic effects. Researchers hypothesize that B[a]P exposure causes an AHR-dependent downregulation of DNA methyltransferases and epigenetic expression changes in genes governing neuromotor development. These studies require substantial tank allocations as they span generations.

Recent Examples of SARL Support for Stakeholder-Driven Research

Industry (Helping Design Safer Products). Manufacturing processes and consumer products collectively release tens of thousands of synthetic chemicals into the environment. No one understands the inherent safety or toxicity of most of these chemicals. The research community needs relevant biological platforms and new computational tools to prioritize the testing of chemicals with limited information about hazards to human health. High-content data from zebrafish evaluated early in the product development pipeline helps the industry to develop inherently safer products (39-41).

Procter & Gamble: Industry has no model to assess the narcotic potency of many chemicals in consumer products. In partnership with Procter & Gamble, SARL researchers developed and validated a 2-day neurobehavioral assay in the larval zebrafish based on a simple test that measures locomotion after a transition

from light to dark. To date, results from over 100 surfactants and numerous combinations in this new neurobehavioral assay were recently published (42). Ongoing collaborative studies are focused on testing reformulations in the zebrafish to empirically improve their product safety.

ICL: The world's largest manufacturer of flame-retardant chemicals approached the SARL with a request to assess proprietary alternative flame retardant chemistries. To date, the SARL has assessed ~75 proprietary formulations for bioactivity in multi-dimensional assays. They have identified several with significantly better safety profiles than current commercially used compounds. These studies provide actionable data that will help the company select and produce inherently safer chemicals. Researchers are also investigating the toxicity mechanisms of the compounds identified as toxic.

Federal Regulatory Agencies (Helping to Identify and Prioritize Environmental Toxicants).
The NIH-funded National Toxicology Program (NTP) recognized the value of interacting directly with a well-established facility core rather than generating a new facility at the NTP campus. For example, the SARL recently screened 3,200 Tox21 chemicals and 80 priority chemicals for the NTP. The SARL screened 91 developmental neurotoxicants (43) and 51 bisphenol derivatives in zebrafish). A recent collaboration between the NTP and the SARL identified a set of "sticky" chemicals that behave aberrantly in the Tox21 *in vitro* screening pipeline. Some sticky chemicals lead to cross-contamination or under-dosing when traditional pipetting was used. The SARL solved this problem with new technology developed at the Hewlett Packard-Corvallis facility. The HP D300 BioPrinter directly dispenses 13 pico-liter droplets into wells using inkjet technology, minimizing error and eliminating losses due to chemical adsorption to the liquid handler (44). The NTP is committed to promoting the advantages of the zebrafish model and standardizing best practices for how to utilize it. NTP has stimulated the formation of a consortium, *Systematic Evaluation of the Application of Zebrafish in Toxicology* (SEAZIT), and identified the SARL as a leader to champion the model and collect data needed to standardize it (45, 46). A current 10 year NIH Battelle subcontract to SARL supports these efforts (see letter of support Barney Sparrow).

The U.S. Environmental Protection Agency (EPA): In collaboration with the US EPA, SARL researchers evaluated all 1,078 EPA ToxCast Phase 1 and 2 compounds in embryonic zebrafish and found that approximately 45% induced significant adverse biological responses (4). The experimental design also revealed a global pattern of responses, defined the concordance between zebrafish and the available *in vitro* and *in vivo* data, and demonstrated that the SARL assays detect adverse responses, such as behavioral effects, that less comprehensive testing strategies miss. The SARL received US EPA priority funding to evaluate the toxicity of per and polyfluoroalkyl substances (#83948101).

Military Laboratories (Helping Detect Environmental Threats and Control Environmental Pollution).
The US Army Center for Environmental Health Research at Fort Detrick, MD, approached the SARL in 2015, having recognized our leadership in zebrafish automation. The Army sought to acquire in-house capabilities for rapid and sensitive detection of chemical bioactivity, especially in the drinking water for active troop deployments. The SARL staff built and delivered to the Army *1*) our automated instrument platform for the 24 hpf embryo photomotor response assay, *2*) our automated dechorionation platform, and *3*) our second-generation robotic platform for placing embryos into 96 well plates. The SARL staff provided protocols to the Army and helped optimize their in-house operations.

The U.S. Army Engineer Research and Development Center (ERDC) approached the SARL wanting predictive zebrafish toxicity models of environmentally persistent high-nitrogen (high-N) compounds from munitions use (47). The SARL helped ERDC to establish its own zebrafish facility and to study the developmental hazard of high-N compounds. The SARL is currently conducting a multi-generational study of tri-nitro-toluene (TNT), a major constituent of munitions, to determine whether developmental effects correspond to epigenetic marker changes in relevant genes.

SARL researchers as Academic Partners for Innovation. The NIH Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, aim to support the development of technology that has a strong potential for commercialization to develop life-saving technologies, and to create jobs. The SARL is a strong supporter of researchers interested in the SBIR and STTR programs. For example, The Tanguay lab is the academic partner for a SBIR grant (R44 OD024879) with Ramona Optics entitled "Parallelized Imaging and Automated Analysis of Zebrafish Assays with a Gigapixel". This phase II grant will use high-throughput optical microscopy and micro-camera array (MCAM) microscopes to capture video with up to 1 gigapixel per frame, which can resolve hundreds of freely-swimming organisms at near-cellular-level detail (5 μm/pixel). Ramona Optics, with the SARL, will produce a suite of software that takes full advantage of the MCAM's resolution and speed to create algorithms to compute larval zebrafish morphological endpoints, speeding up toxicology experiments by 100X over current screening methods. SARL researchers are engaged with several other companies as the academic partner for SBIR and STTR grant submissions. Modernization of the SARL engineering space will facilitate future innovative partnerships.

In summary, the scope and diversity of NIH and stakeholder-supported research supported by the SARL require a modern research space, high-quality water, efficient fail-safe life support system, flexible rack systems, improved researcher access, and all with improved sustainability. *SARL is at a critical junction with outdated infrastructure and a growing inability to meet expanding researcher needs.*

Management and Key Personnel. The PI, Dr. Tanguay, has her office and research laboratory located in the SARL so she is positioned well to oversee the project. Dr. Tanguay will work closely with the following key personnel to oversee the planning and project execution: Mr. Lowell Fausett, the Oregon State University College of Agriculture Architect, has over 35 years of laboratory design work, project management, and construction expertise, Mr. Fausett specializes in laboratory renovations with a breadth of knowledge of diverse construction materials and methods. Lowell is well known and respected in the construction community and is particularly adept at working through existing constraints inherent in remodeling. His in-depth knowledge of mechanical and electrical systems helps in developing economical solutions while maintaining a high level of quality. Mr. Fausett is a master at getting the job done on time and on budget. Mr. Eric Johnson, SARL Facility Manager, has worked on-site for over 25 years. Eric has aquatic models, mechanical, electrical, engineering, plumbing, welding, and facility maintenance expertise and will coordinate the water supply and life support final design, installation, and final commissioning. He will also be responsible for operational maintenance after project completion. He will coordinate with Tecniplast the capital equipment specifications, installation, and operations. This team has worked together for nearly two decades to design and execute renovations of the other SARL wings. The multi-media SARL conference room will serve as the Construction office for this project.

DEVELOPMENT OF THE FACILITY

Renovate the existing unused 3,500 sq. ft North Wing of the SARL facility

The North Wing is currently empty and not in use. This location was intentionally selected to ensure the proposed construction and renovation will not hamper daily operations of this important facility. Detailed demolition drawings will be developed during the SD and DD phases of the project. No significant challenges are expected with the demolition process. Once the project is completed and commissioned, the existing obsolete zebrafish housing facility will be decommissioned and renovated for other purposes using institutional resources. The proposed SARL north wing renovation and expansion provides additional housing capacity for zebrafish and much needed support spaces such as tank washing facilities, prep labs, imaging lab and an expansion of the water treatment mechanical room (*see in **Other Attachments - Figure 1**: Overall Site Plan)*. The 3,500 gross sq. ft. facility will be designed to meet BSL-2 requirements with additional security and operational protocols to function as an microsporidia-specific pathogen-free (SPF) facility. (*see **Other Attachments- Figure 2**: North Wing Conceptual Plan)*

Architectural

Site Work: The is an entirely a renovation project that will not add any new sqare footge to ther exiting SARL footprint. Landscaping around the renovated north wing will include drought-resistant plant materials and ground cover.

Site Utilities: No major upgrades to existing utilities are anticipated.

Building Construction: The deteriorated roof of the existing 40 year old pre-fabricated, steel framed metal building will be replaced to improve internal ceiling height clearance from a low point of 5'-6" to 14'-0" clear. This will allow for a finished ceiling height of 10'-0" AFF and adequate space above for mechanical ductwork ***Other Attachments - Figure 3:*** *Conceptual Elevation Plan*). The original corrugated metal siding will be replaced with a concrete masonry unit (CMU) wall with 2" of extruded polystyrene adhered to the exterior surface to achieve the required R-13 insulation value. The polystyrene insulation will be covered with a rain screen system including an engineered water intrusion wrap sheet material, vertical furring, building paper and an exterior skin of formed metal panel. The internal shear wall along the main corridor will be concrete as well.

The new roof of the building will be an insulated metal standing-seam system, sloped to perimeter gutters and downspouts to minimize the need for roof penetrations. The west facing roof will be designed to support a future solar panel array (***see Other Attachments - Figure 4****: Conceptual Roof Plan*). Rooftop mechanical equipment zones located on the east side of the building will be enclosed and the required free area for ventilation will be provided through metal louvers in the exterior wall system. Exhaust fans stacks will penetrate the insulated metal standing-seam system.

The building will be insulated to a minimum of R-13 for the exterior walls and R-19 for the roof.

Exterior Envelope:	CMU wall and metal panel and entry canopy
Roof:	Single-ply PVS membrane roofing, 60 mils. thick.

Zebrafish Housing and Support: Interior finish materials within the zebrafish holding room will be selected for long-term durability and ease of cleaning. Perimeter walls within the facility will be constructed of 6" CMU sealed with block filler and a three-coat reinforced epoxy wall system. Ceilings will be constructed of gypsum board over metal framing sealed with a three-coat epoxy paint system. Floors will be concrete covered with a troweled-on epoxy floor system with integral coved base.

All corridors within the renovated area will have a clear width of 7'-0". A 6" canted concrete base will be provided in the corridors to prevent damage to the walls from movement of racks and other equipment. Doors within the zebrafish holding area will have a minimum clear width of 48" and are to be stainless steel, solid core doors and fully grouted frames with door gasketing. Stainless steel plating will be installed on the lower half of each animal holding room door to prevent damage from movement of racks.

Casework will be powder-coated metal. Countertops will be epoxy resin and stainless steel with integral stainless steel sinks and a raised lip at the exterior edge to contain spills. Fixed base cabinets will be set on a 4" concrete housekeeping pad.

Detailing of surface and material intersections will be given special attention to support cleaning and maintenance goals.

Labs and Associated Support: All lab and lab support spaces have been located across the hall from the zebrafish holding room to isolate noise and vibration from animal holding areas. Services have been centrally located to provide maximum efficiency and materials flow in and out of the facility.

Sustainability

It is OSU's policy that all major building projects be designed to meet LEED Silver certification status. The SARL building renovation will be designed to meet this criteria for certification standards under the US Green Building Councils LEED for New Construction and Major Renovations. The complexity of systems requirements for a vivarium present a unique set of challenges for energy efficient and sustainable design. Therefore, our main focus will be to develop strategies to conserve water and improve energy conservation. The mechanical equipment serving this wing of the building will be right-sized based on a careful analysis of heat loads from equipment and animals. The design team will work together to balance the requirements for animal and staff health and safety with the goals of highly efficient systems design and energy efficiency.

Mechanical

Dedicated supply and exhaust systems with 100% redundancy will be provided for the north wing of the building. Air handlers located within the mechanical room will provide 100% outside air, after conditioning, to all aquatic holding rooms and associated lab support spaces. All spaces within the renovated area will be fully exhausted. Aquatic animal holding rooms and associated support spaces will be designed to meet NIH standards with individual temperature controls, air volume controls, humidity controls and 15 air changes per hour. Animal holding rooms will be negatively pressured relative to the adjacent corridor. The HVAC system will supply sufficient conditioned non-recirculated air to all aquatic animal holding rooms to maintain relative humidity in the range of 30-60% and dry bulb temperatures at 80°F (+/-2°F). Two sets of air filter banks will provide not less than 30% filtration at the pre-filters and 95% at the final filters. Each aquatic animal holding room will have its own temperature and air volume monitoring and control system. Heat recovery will be provided at all general exhaust outlets.

Plumbing

The plumbing system will be designed to match that of the existing SPF facility. Hand-wash sinks, emergency showers and eyewash stations will be located in the ante room provided for each pod of six animal holding rooms.

Fire Protection: The north wing of the building will be completely sprinklered using a conventional wet pipe system with zone control valves to segment the system. A double check valve backflow device will be used on the incoming service and a main riser will be provided. Sprinkler heads will be recessed.

Plumbing Fixtures: The plumbing fixtures will be commercial grade and provided with water efficient valves. Hose reels will be provided in each aquatic animal holding room for wash down.

Electrical

Electrical: Normal power will be served by a new 277/480 volt main electrical. The existing emergency generator has adequate capacity to support all systems in the renovated north wing. The existing automatic transfer switch and emergency panel boards will be used to support this space. Security door switches/contacts will be provided for all exterior doors. All outlets within the aquatic animal holding rooms will be heavy duty GFI duplex receptacles with a weatherproof cover.

Lighting: New lighting will consist of 1'x4' LED fixtures that provide an average dual light level of 30 foot candles in the animal holding rooms and 70 to 75 fc in the labs and lab support spaces including cage washing. Automatic time-clock control and a manual timer switch control will be provided for each animal holding room. Manual switches will be provided for all other areas. The LED lighting fixtures within animal holding areas will be sealed and waterproofed.

Emergency Power: A dedicated building generator is already in place to provide emergency power to all life-safety loads and code required standby loads. It is sized to maintain minimal air exchange rates, temperature between 70 to 76 degrees F, and tank systems. Emergency egress lighting will be provided to maintain a minimum of one (1) foot-candle at the floor and to meet all State and local Code requirements.

Low Voltage: New fire alarm devices will be provided to meet NFPA requirements. Telephone outlets will be provided in the corridor with conduits and pull string to the communications room. All external doors will be secured utilizing magnetic locks and proximity card key readers. The card key readers will be connected to the main office in the existing building and at the main campus security office.

Commissioning: Systems to be commissioned are noted below:
HVAC: Chilled water system, heating water system, air handling units, terminal units, reheat coils, DDC controls.
Electrical: Lighting control system, occupancy sensors, power monitoring system.
Plumbing: Gas water heaters, mixing valves, return pumps, trap primers, grey-water system
Renewable energy: Solar heating water system, solar panel array and controls.

Detailed Description of current limitations and proposed solutions.

The following section defines the current facility needs, capabilities, and significant limitations followed by projections of how successful completion of this modernization project will address limitations to meet current and future zebrafish biomedical research needs.

Engineering and technology innovation space

Existing situation and limitation. Instrument development is a hallmark of SARL activities. SARL engineers currently utilize a disconnected portion of the SARL. A computer numerical control (CNC) router, 3-D printer, electronics workshop, and instrument assembly reside in this space.

Proposed solution. We propose to build an engineering suite adjacent to the current SARL shop to accommodate engineer projects. This space will have appropriate electricals and a fire suppressing system as detailed in the above construction overview.

Specialized Use Housing Rooms

Existing situation and limitation. SARL researchers often require flow-through, non-standard photoperiod capabilities to support chemical exposure or specialized dietary experiments, as this water cannot return to the recirculating system. The SARL has only one small room dedicated to this space, greatly limiting researcher access. This room uses water from the undersized fish room sump and the exposure tanks are on tables instead of efficient racks. The room has poor ventilation and the climate control is provided by inefficient and unsafe electric heat and a portable A/C unit. The room cannot accommodate different photoperiods, greatly limiting experimental design.

Proposed solution. As part of the demolition, we propose to eliminate the existing room and replace it with two smaller specialty rooms. Each room will be under modern HVAC control, have floor drains and sanitizable surfaces. One room will permit multiple, simultaneous experiments with fish on different day/night cycles. The second specialty room will have a simpler standalone open rack. Both rooms will have a dedicated user workspace for visiting facilty users. The newly installed life support system sump water will deliver incoming rack water

using timed episodic water exchanges, taking advantage of the appropriate temperature water from the oversized main life support system. Finally, redundant chemical capture filtration will treat the outflow water.

Capital Equipment

Below we describe requested Capital equipment needs. Tecniplast was chosen as the principal supplier due to their 45+ years of experience producing high-quality laboratory animal housing and life support systems. They emphasize one-of-a-kind integration of robotic technologies to improve animal welfare and increase daily operating efficiency and research productivity. In addition to having a wide range of specialty products designed specifically for the needs of a modern biomedical aquatic research laboratory, they have also incorporated remote access technical support systems on all equipment including life support, robotic feeding, and tank washing. In addition to real-time monitoring, regional highly trained technical support and personnel are available to be onsite within 24 hours.

Recirculating zebrafish life support systems

Existing situation and limitation. The SARL currently has two significantly undersized recirculating life support systems originally designed by Aquaneering, Inc. These systems are over 15 years old, inefficient, expensive to maintain, and are failing. These two systems are supplying water to a total of 24 single-sided small racks and 30 mass spawning tanks in three different rooms. Additionally, water is removed from the sump to supply water for a specialized flow-through room for researchers to conduct dietary and chemical exposure experiments, as well as three separate quarantine isolation rooms, where water cannot go back into the recirculating sump. The Aquaneering systems lack integrated charcoal purification, the particulate filtration requires daily manual disposable replacement, and the system monitoring and alarm systems are unreliable. Finally, the sump chamber itself is powder-coated aluminum that has reached the end of its life and is leaching materials into the fish water.

Proposed solution. We propose to install a modern appropriately sized life support system designed by Tecniplast. The Tecniplast Central Life Support (CLS) system utilizes several processes to ensure the highest level of water sanitation for optimal fish health. These include a 36 micron mechanical drum filter with automated cleaning and backwash to remove solid waste. Biological filtration will be achieved using a low maintenance/high efficacy fluidized bio-chip bio-filter. The CLS system will be equipped with a high-efficiency pass-through pressurized vessel containing acid-washed neutral pH carbon material in 50-100 micron filter socks. This will allow for the effective removal of dissolved organics and potential toxins within the re-circulating system. Disinfection will be achieved via an ultra violet (UV) disinfection unit that provides a UV-C dose of >150,000 mW/cm^2 at end of bulb life. The UV chamber is made of AISI316L stainless steel, a surface that increases the effective UV by reflecting light rays and increasing the disinfection power. AISI316L stainless steel, when compared to plastic, provides longer durability. The system will be driven by redundant variable frequency circulation pumps, with whisper technology to reduce noise levels. Submerged heater elements provide additional levels of temperature control. All water exchange processes are automated and timed over 24 hours for increased water quality and condition stability. The CLS system provides constant water quality monitoring, control, and dosing for pH, conductivity, temperature, and total dissolved solids. The entire system is controlled from a user-friendly touch screen control center which includes passcode access for remote monitoring and operation thus providing complete system management. The control center also allows for customizable push notifications as an additional safeguard.

Zebrafish housing systems

Existing situation and limitation. The current obsolete 24 small single-sided racks are distributed in three disconnected small rooms in short 2-3 rack rows. These current rooms are not wheelchair accessible as they are on different floor elevations. The current racks require users to turn valves off to move tanks, and these valves frequently fail. The existing racks also lack tank location locks, which can cause incorrect racking or out of position errors. With an increasing number of mutant and transgenic lines, there is a need for specialized pair spawning and genotyping racks that allow animals to remain on flowing water for increased quality of care. Finally, the current racks cannot accommodate larger populations of common lines for on-rack spawning.

Proposed solution. We propose to replace obsolete housing racks by installing 18 larger Tecniplast racks with seismic bracing. These racks have simple push and pull nozzles with a fine-tune inlet flow control. Each valve will have visual indicators of water delivery, thus optimizing daily animal welfare and system assessment. The racks have the flexibility to hold a variety of tank volumes, with blue-colored tanks and lids to reduce algae growth. The new tanks incorporate a V-channel bottom, rounded corners, sloped from front to back to funnel debris to a siphon for automatic cleaning, as well as optional perforated dividers to divide populations without removing them from a home tank. The racks include innovative 16-liter Z-Park tanks which permit high-density housing on standard racks and automatic feeding. Importantly, specialized dividers allow for spawning on racks, which reduces animal stress and staff time. The tanks provide fish enrichment with integrated gravel-like tank bottoms.

Zebrafish Feeding Process

Existing situation and limitation. The existing 2,000 zebrafish tanks are distributed into three separate small rooms in short rows and are manually fed three times daily by SARL staff, 365 days a year. The consistency of feeding by staff is difficult to ensure and salary and benefit costs continue to threaten its long-term sustainability. There is a significant volume of wasted feed with manual feeding as well as constant sanitation issues.

Proposed solution. With the arrangement of two contiguous rows of Tecniplast racks, we propose to install two Tecniplast Tritone automatic feeding systems to automate daily fish feeding. This system integrates perfectly with the rack system and can precisely deliver up to four different pellet sizes and liquid diets to accommodate different life stages and dietary needs of specialized lines, several times per day and over a longer range of hours than staff can physically be in the building. In addition to better normalization of feeding, which will improve cleanliness and water quality, the installation will substantially improve employee safety by significantly reducing the need for ladders. The Tritone automatic feeders can also be remotely operated in the event of disrupted building access. The Tritones operate by scanning a QR code on a tank label, and the robots can log data and can provide a daily tank census automatically.

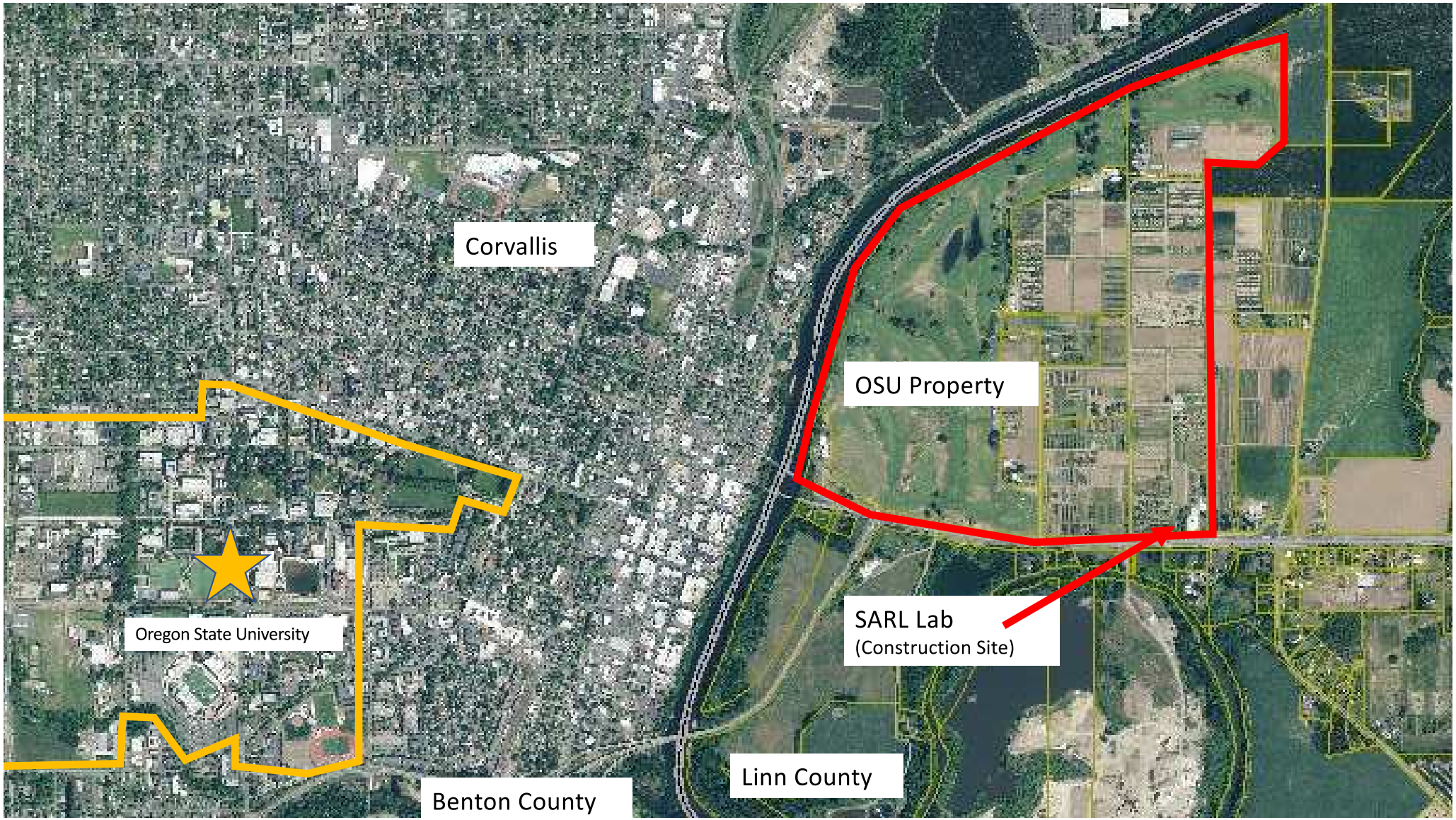
Tank washing capabilities

Existing situation and limitation. Our existing facility has a relatively new single Tecniplast 650A cage washer and a small undersized commercial dishwasher located within the obsolete zebrafish facility. To maintain our SPF status, we wash hundreds of tanks a week, which requires numerous wash cycles and is labor-intensive. Additionally, the existing dishwasher is unable to accommodate smaller item such as tank baffles, etc. Finally, the location of the existing tank washing system is too far from the proposed SARL North Wing renovation for feasible use.

Proposed solution. To meet tank-washing throughput needs, we propose to construct a tank washing room with clean and dirty pass-through sides that will allow us to relocate the Tecniplast 650A cagewasher. We also request the support to purchase a smaller Calypso tank washer to handle small tanks, and smaller accessories. The requested Calypso system will be dedicated to smaller aquatic accessories, requires only electricity and water, no need for exhaust, thus reducing HVAC demands. Both tank washing systems are equipped with remote monitoring and technical support access, as well as data collection and reporting systems.

SUMMARY

The SARL has supported NIH researchers for over fifty years by adapting to current and future researcher needs. OSU leadership recognizes the importance of this facility to achieve campus strategic goals in the science of sustainability health and wellness, and economic prosperity and social progress. With the exponential growth in the campus zebrafish NIH biomedical research base over the past decade, accomplishing the deliberate SARL renovation and modernization will serve as a critical resource to support biomedical research for another fifty years and beyond.


Corvallis
OSU Property
Oregon State University
SARL Lab
(Construction Site)
Linn County
Benton County

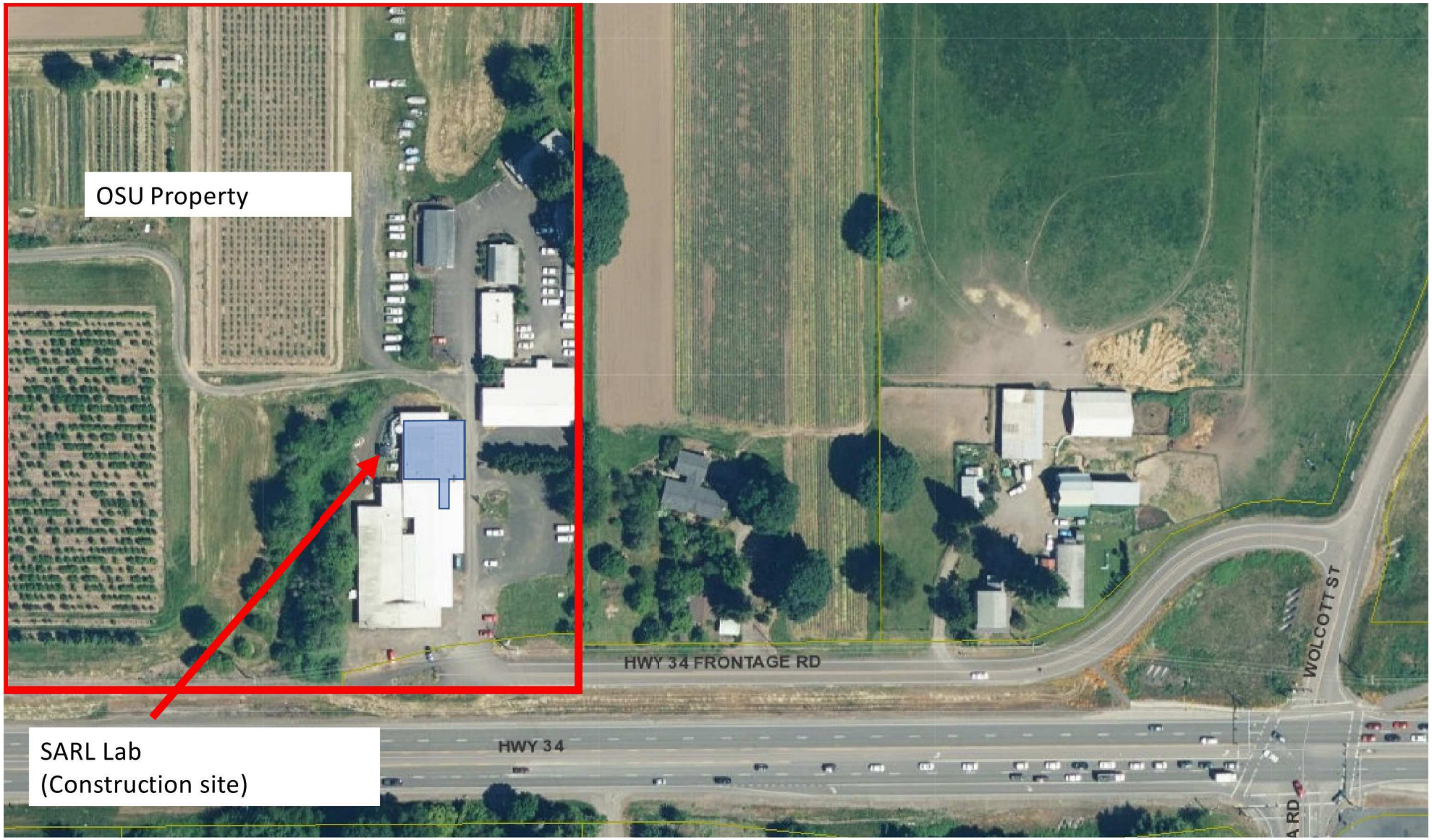
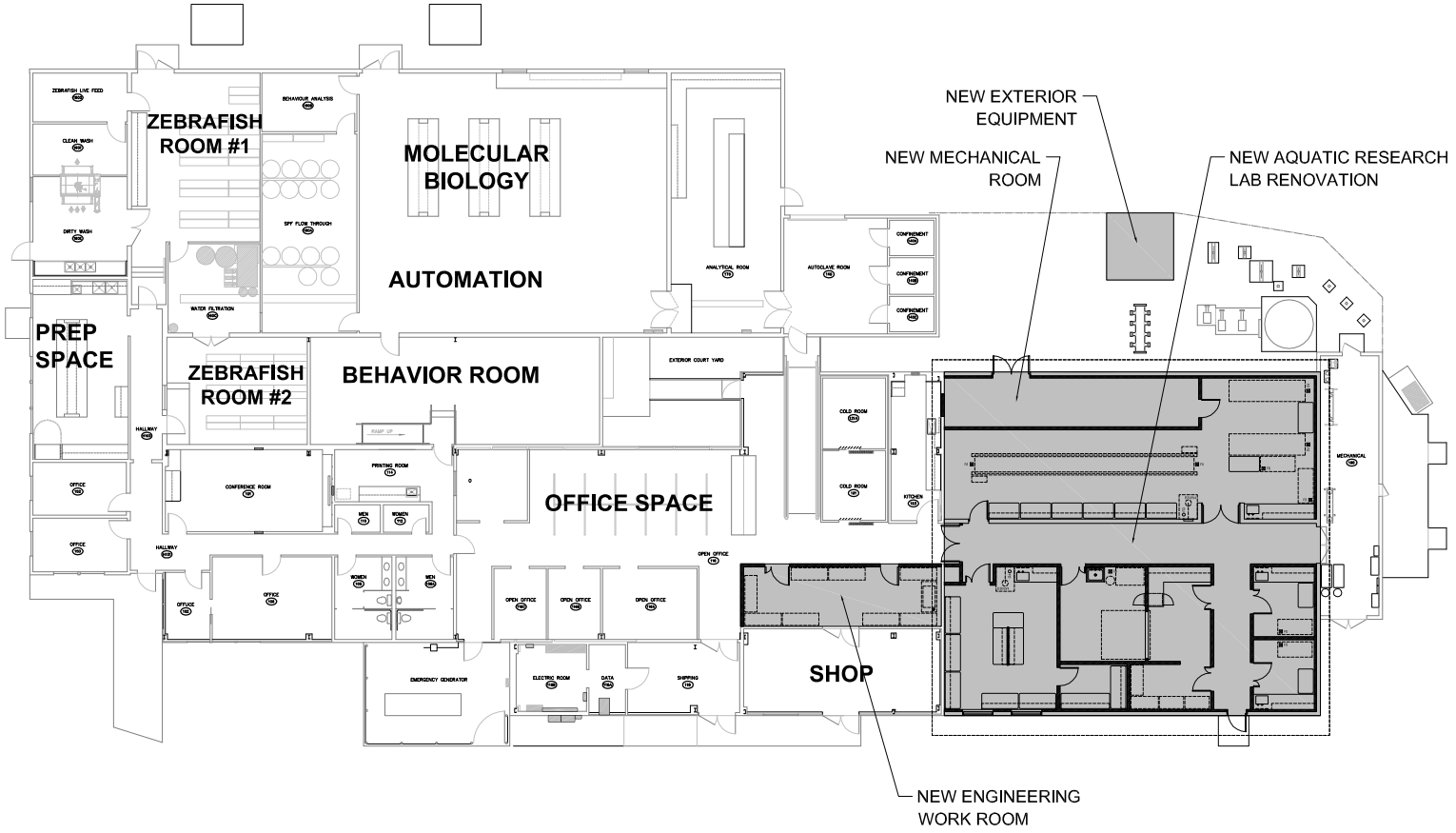

OSU Property
SARL Lab
(Construction site)
HWY 34 FRONTAGE RD
HWY 34
WOLCOTT ST

FIGURE #1 - OVERALL SITE PLAN



1 / LF1.0 SITE PLAN / OVERALL FLOOR PLAN

SCALE: 1" = 30'-0"

N

ESTIMÉ

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OSU Sinnhuber Aquatic Research Laboratory
28645 East Highway 34, Corvallis, OR 97333
SITE PLAN / OVERALL FLOOR PLAN

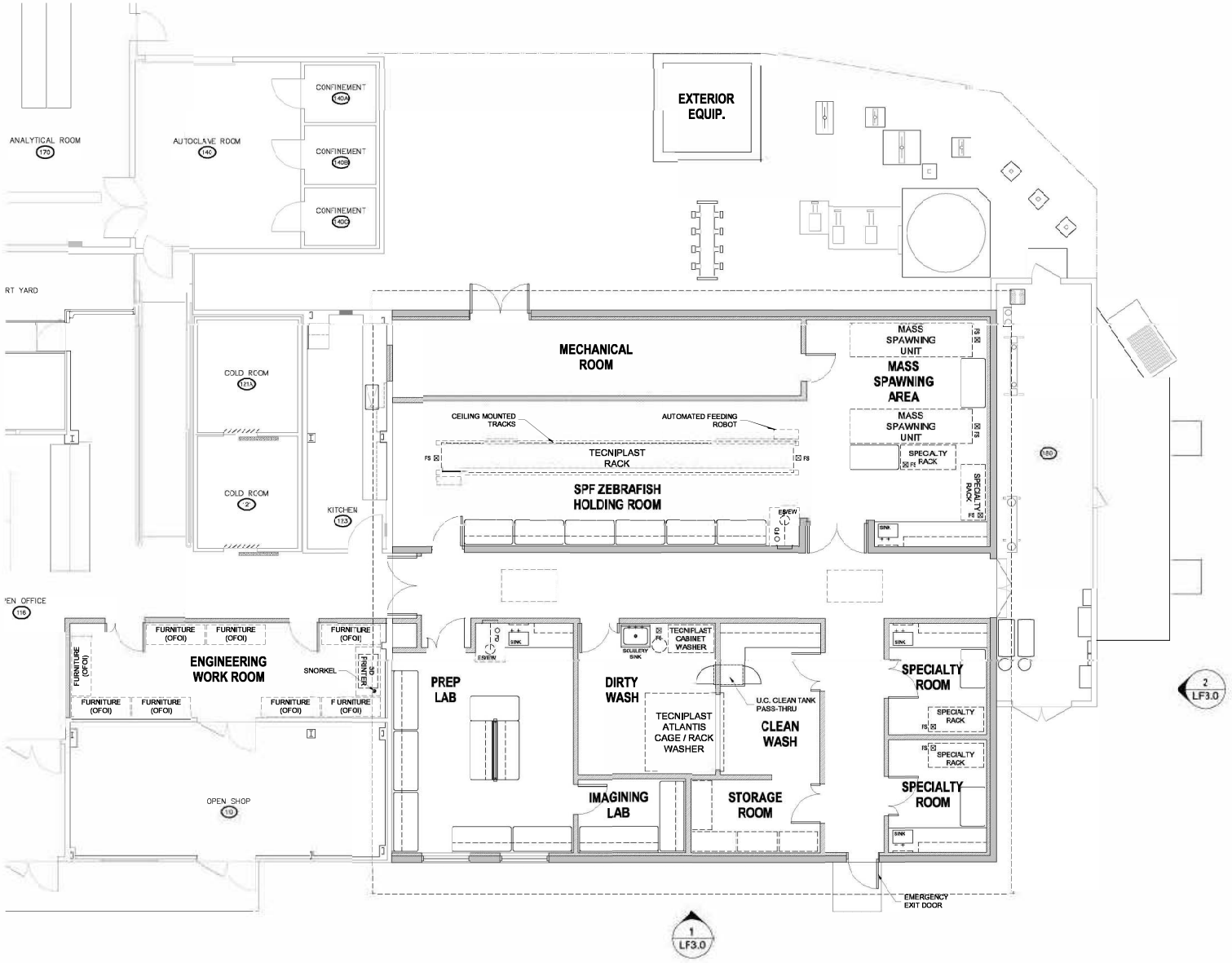
Date: FEBRUARY 7, 2023

Scale:

Drawing No.

LF1.0

FIGURE #2 - NORTH WING CONCEPT



1 LF2.0 NORTH WING CONCEPTUAL RENOVATION & ADDITION PLAN

SCALE: 1/16" = 1'-0"

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OSU Sinnhuber Aquatic Research Laboratory
28645 East Highway 34, Corvallis, OR 97333
NORTH WING CONCEPTUAL RENOVATION & ADDITION PLAN

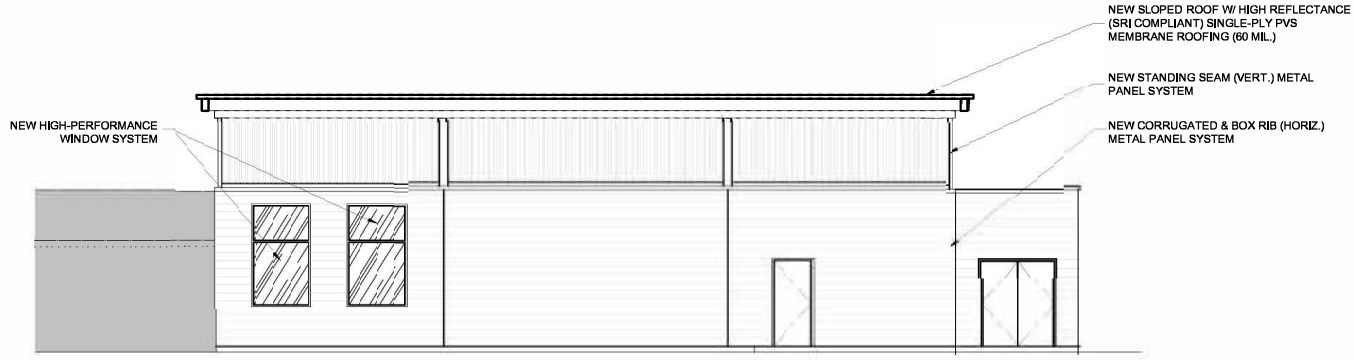
Date: FEBRUARY 7, 2023

Scale:

Drawing No.

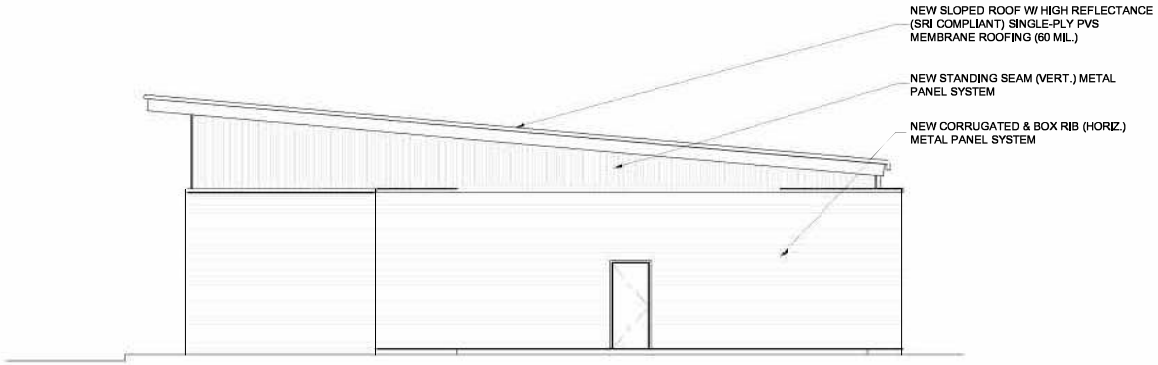
LF2.0

FIGURE #3- ROOF ELEVATION PLAN



1 LF3.0 EAST CONCEPTUAL ELEVATION

SCALE: 1/16" = 1'-0"



2 LF3.0 NORTH CONCEPTUAL ELEVATION

SCALE: 1/16" = 1'-0"

ESTIMÉ

The Estimé Group
P.O. Box 11712
Bainbridge Island, WA 98110
P (206) 428-3777

OSU Sinnhuber Aquatic Research Laboratory
28645 East Highway 34, Corvallis, OR 97333
NORTH WING CONCEPTUAL ELEVATIONS

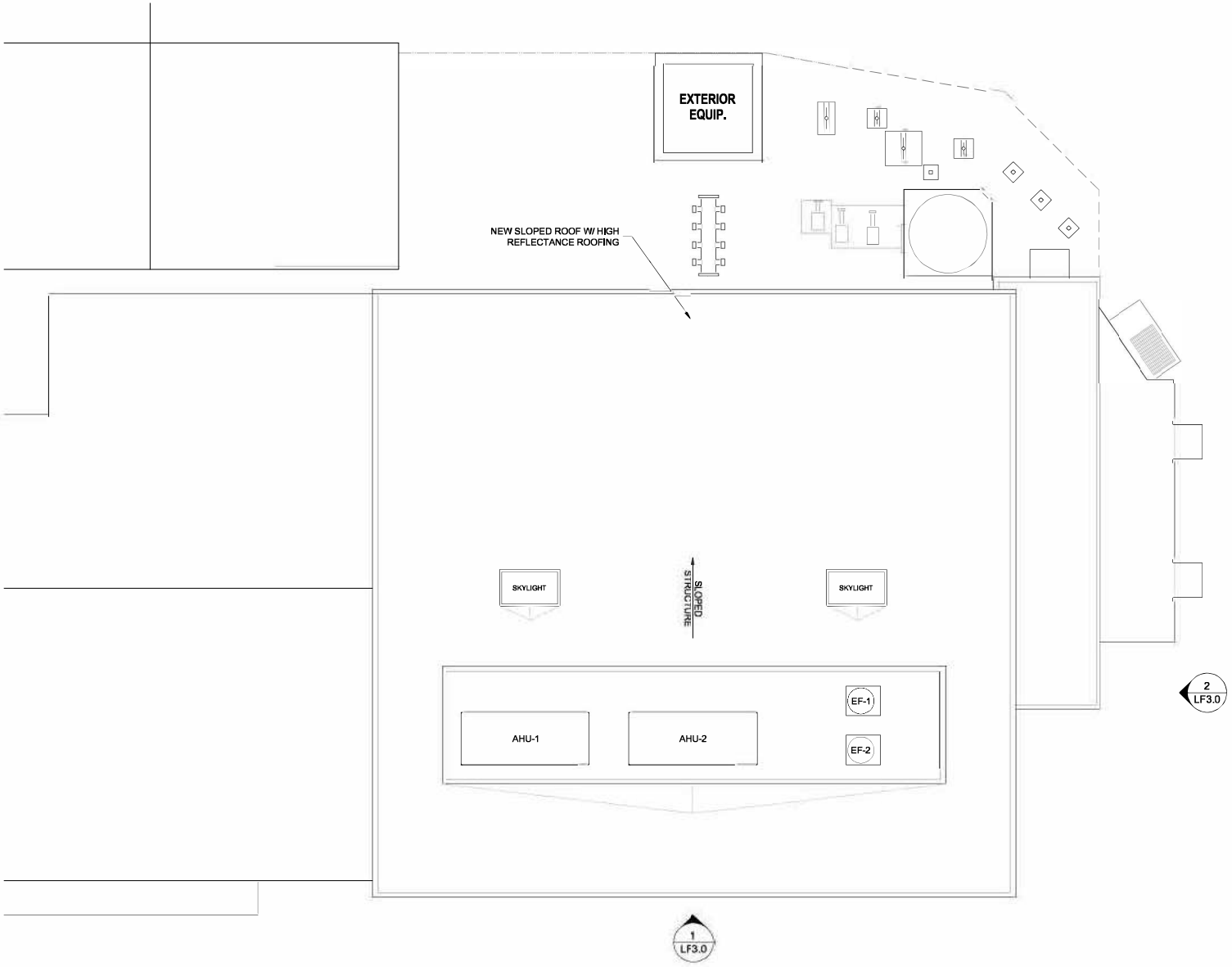
Date: FEBRUARY 7, 2023

Scale:

Drawing No.

LF3.0

FIGURE #4 - NORTH WING ROOF PLAN



1 LF2.1 NORTH WING CONCEPTUAL ROOF PLAN

SCALE: 1/16" = 1'-0"

ESTIMÉ

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NORTH WING CONCEPTUAL ROOF PLAN

Date: FEBRUARY 7, 2023

Scale:

Drawing No.

LF2.1

Oregon State University - Sinnhuber Aquatic Research Laboratory
North Wing Renovation - Space Program

	Space Type	Qty	Depth	Width	Room Net Area	Total Net Area
A.	**Aquatics Holding Room**					
A.1.	- SPF Zebrafish Holding Room	1	15	45	675	675
A.2.	- Mass Spawning	1	12.75	14.5	185	185
A.3.	- Specialty Holding/Work Area	1	10.75	13.75	148	148
A.5.	*Holding Rooms - Sub-Total*	*3*				*1,008*
B.	**Lab & Support Spaces:**					
B.1.	- Specialty Lab	2	10	12	120	240
B.2.	- Prep. Lab	1	18.25	23.25	424	424
B.3.	- Imaging Lab	1	7.5	13.75	103	103
B.4.	- Dirty Wash	1	14	15	210	210
B.5.	- Clean Wash	1	10.75	15	161	161
B.6.	- Storage Room	1	7.5	13.75	103	103
B.7.	- Engineering Work Room	1	10	33	330	330
B.8.	*Research - Sub-Total*	*8*				*1,572*

Total Net Area			**2,580**
Assume 74% Building Net-to-Gross Efficiency		74%	
Estimated Gross Building Area			**3,500**

Table 2 - Requested Fixed Equipment

Item Name	Manufacturer	Model #	Total Cost	Location in Facility	Quote Attachment #
Life Support System	Tecniplast	Customized	$518,838	Mechanical Room	Quote 1
Main Room Rack System (18)	Tecniplast	ZB3060DXH; ZXB3060SXH	$298,825	SPF Zebrafish Holding Room	Quote 1
Tritone Automatic Feeders (2)	Tecniplast	Tritone	$301,138	SPF Zebrafish Holding Room	Quote 1
Calypso Tank Washer System	Tecniplast	Calypso	$69,904	Tank Washing Room	Quote 2
Real-Time Monitoring System	Tecniplast	Real View 3	$11,353	Facility Wide	Quote 2
		Fixed Equipment Total	**$1,200,058**		

Table 3 - List of Active NIH Grants Directly Related to Project

Funder	Grant #	PI Last Name	Title	Annual DC ($)	Funding Period
NIEHS	P42ES016465	Tanguay	PAHs: New Technologies and Emerging Health Risks [***Parent Grant***]	$1,928,434	02/01/2020 - 1/31/2025
	P42ES016465-5003	Smith	Elucidating Metabolic and Physicochemical Mechanisms of PAH Susceptibility in Toxicity Test Systems and Humans	$205,000	02/01/2020 - 1/31/2025
	P42ES016465-5004	Tanguay	Predicting the Toxicity of Complex PAH Mixtures	$205,000	02/01/2020 - 1/31/2025
	P42ES016465-5005	Simonich/Semprini	Identification of Remediation Technologies and Conditions that Minimize Formation of Hazardous PAH Breakdown Products at Superfund Sites	$205,000	02/01/2020 - 1/31/2025
NIEHS	P30ES030287	Ho/Tanguay	Pacific Northwest Center for Translational Environmental Health Research [***Parent Grant***]	$774,091	07/1/2020 - 03/31/2025
	P30ES030287	Truong	Zebrafish Biomedical Research Facility Core	$73,593	07/1/2020 - 03/31/2025
NIEHS	R01ES033888	Hahn	Mechanisms Controlling Sensitivity and Resistance to Dioxin-like Compounds: Role of AIP	$328,923	09/07/2022 - 08/31/2027
NIDCD	R01DC014588	Johnson	In Vivo And In Vitro Studies Of The Deafness Associated Protein Otoferlin	$250,000	02/01/2020 - 1/31/2025
NIEHS	R21ES033753	Rothenberg	Parental Co-Exposure to Methylmercury and Inorganic Arsenic in Zebrafish (Danio Rerio): Metabolism and Offspring Behavior	$125,000	09/15/2022 - 08/31/2024
NIEHS	R01ES032707	Semprini	Development of Passive and Sustainable Cometabolic Systems to Treat Complex Contaminant Mixtures by Encapsulating Microbial Cultures and Slow Release Substrates in Hydrogels	$200,000	12/16/2020 - 10/31/2025
NIEHS	R01ES030226	Sharpton	Impacts Of Benzo[A]Pyrene On Microbiome Development Across Lifespan And Generations And The Behavioral Consequences	$281,743	02/01/2019 - 01/31/2024
NIEHS	R35ES031709	Tanguay	Discovering Chemical Activity Networks - Predicting Bioactivity Based on Structure	$750,000	04/1/2021 - 03/31/2029
NIEHS	R44OD024879	Harfouche	High-Resolution, Parallelized Imaging of Freely Swimming Zebrafish with a Gigapixel Microscope	$130,500	07/15/2017 - 05/31/2023
NIEHS	U01ES027294	Tanguay	Multidimensional In Vivo Assessments Of Engineered Nanomaterials And Biological Interactions	$161,863	09/30/2016 - 08/31/2023
NIEHS	R01ES033243	Wright	Characterizing Gene-Environment Interactions that Affect Individual Suspectibility to an Expanding Chemical Exposome	$80,000	7/8/2022 - 4/30/2027
			Annual Total Direct Cost	**$4,601,631**	

OSU - SARL NORTH WING RENOVATION

PROPOSED PROJECT SCHEDULE

Project Phase	Duration (months)	10/1/23 - 12/31/23	1/1/24 - 3/31/24	4/1/24 - 6/31/24	7/1/24 - 9/30/24	10/1/24 - 12/31/24	1/1/25 3/31/25	4/1/25 - 6/31/25	7/1/25 - 9/30/25	10/1/25 - 12/31/25	1/1/26 3/31/26
Schematic Design	2										
Design Development	3										
Construction Document	3										
Bidding/Negotiation	2										
Construction	15										
Commissioning	2										
Contractor Selection	2										