1 ACCESS TO CBCS SERVICES

1.1 KEY CRITERIA FOR ENABLING BROAD ACCESSIBILITY

CBCS services must be accessible on equal terms to all Swedish academic users interested in using the chemical biology tools provided by CBCS. Services may also be accessible to international academics and non-academics (the private sector, healthcare, and governmental agencies) based on a full-cost coverage model. CBCS reserves the right to prioritize resources for Swedish academic users, and the Project Review Committee (PRC) will prioritize resources for all ongoing and planned projects bi-annually. CBCS resources must be allocated to projects based on an objective and transparent evaluation to ensure fair and equal access to services. The key parameters currently considered are scientific potential and impact, and technical feasibility. Additionally, users must demonstrate sufficient funding to support their parts of the collaborative project. See Table 2 below for a description of the user type and cost model:

Table 1. Summary of CBCS accessibility to different user types, how they are prioritised, and cost model.

User group	Applicant	Priority set by	Cost model
Swedish academics	Researcher	PRC*	Subsidized
	Researcher with CBCS as co-applicant to any funding agencies	PRC	Full cost
International academics *Max 20% of CBCS resources*	EU-OPENSCREEN	PRC	Full cost
	Other contacts	PRC	Full cost
	Researcher with CBCS as co-applicant to any funding agencies	PRC	Full cost
Non-academic *If resources available*	Private sector (national and international)	First come – First served	Full cost
	Healthcare and gov agencies	First come- First served	Full cost
	Charity organizations	First come - First served	Full cost

* PRC – Project Review Committee

1.2 COLLABORATION MODEL

To allocate CBCS resources as objectively and time efficiently as possible, we have established a collaborative project model, including a project prioritization process, that has been in place for over 10 years. CBCS activities are, in most projects, a close collaboration between the researcher and CBCS staff scientists. The aim is to increase the scientific impact by efficiently combining the technical expertise from CBCS with the scientific expertise that the researcher possesses within their research field.

1.2.1 CBCS project types

CBCS project types can be summarized into six groups. In principle, these apply to all categories of services offered at CBCS (see section 3). A detailed description of each project type and user type is listed in Table 3 below.

Table 2. Description of CBCS project types and target users.

Project type	User type	Description	Time	Priority
Consultations/ pre-projects *(Handled at a local node)*	Academic	Intellectual input to projects and limited use of equipment to evaluate project potential.	Occasional hours	First come, first served
	Non-academic*			If resources available
	Int. academic			If resources available
Service projects *(Handled at a local node)*	Academic	Limited lab support Access to compounds from screening collection	~ 2 weeks full-time support	First come - first served if resources are available
	Non-academic*			If resources available
	Int. academic			If resources available
PRC projects	Academic	Need of significant support from staff scientist	Typically, 6 months to 2 years	Set by PRC
	Int. academic	Maximum 10% of project portfolio available for international collaborations	Typically, 6 months to 2 years	Set by PRC
Open access *(Handled at a local node)*	Academic	Users perform experiments on CBCS equipment	Training of users by CBCS staff (hours)	First come - First served
Technical development *(Handled at a local node)*	CBCS Staff scientists	CBCS staff develops relevant techniques in the lab	Max. 20% within the SciLifeLab support	
EU Openscreen *(KI and Umu nodes)*	Academic	The project applied within the EU-OPENSCREEN framework		PRC / If resources available

*Services to non-academic users are only considered if the service requested is not available on the market. Full-cost and reasonable market price is applied, according to governmental regulations.

1.2.2 Project onboarding and development scenarios

The majority of CBCS resources are used in projects for assay development, screening, and enabling chemistry. The onboarding process of these projects is shown in Figure 3. In recruiting new potential users of the infrastructure, CBCS meets with principal investigators (PI) or representatives from their research groups. These **consultation meetings** are intended to provide an overview of the infrastructure capabilities, listen to the project proposal, and evaluate the potential to initiate collaborative projects. Also, the user is informed how costs are divided between the PI and the infrastructure.

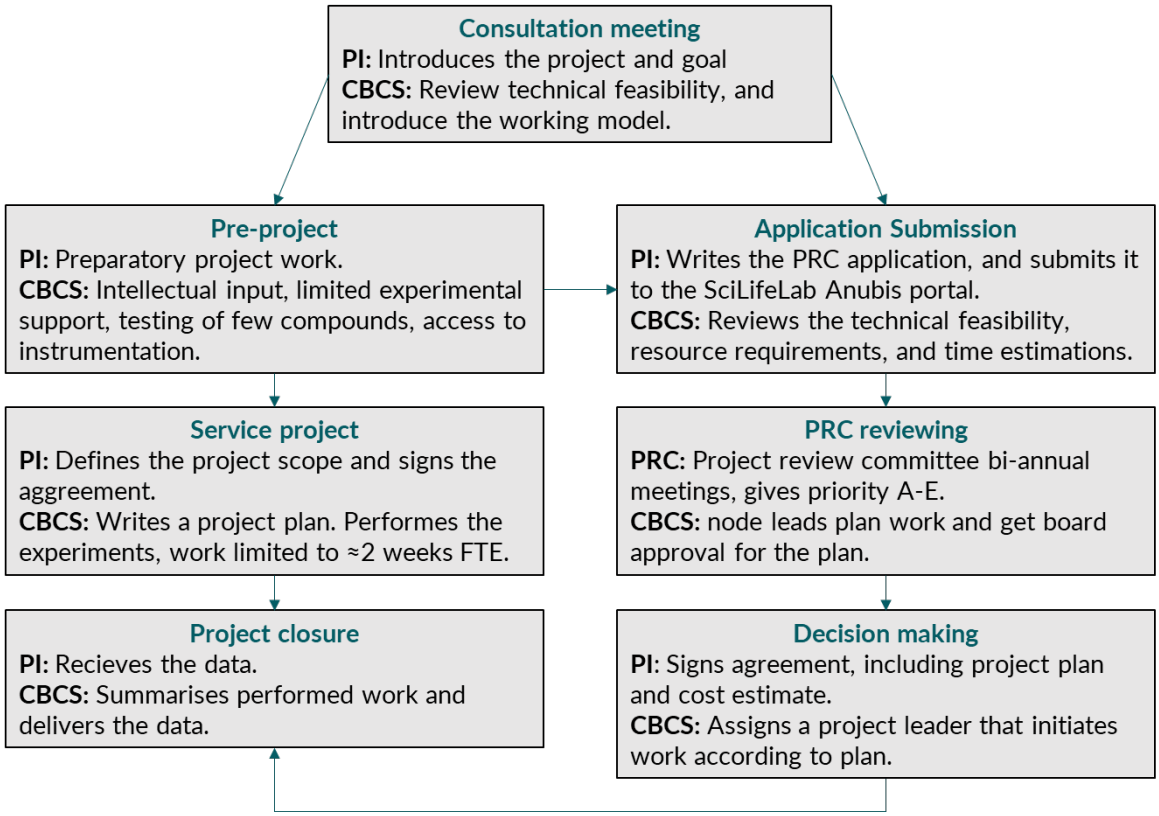

Figure 3. Project routes at CBCS.

Pre-projects include intellectual support by CBCS regarding assay design and screening concept. In some cases, CBCS provides limited sets of compounds for testing relevant hypotheses or evaluating an existing assay. The interaction may also involve access to appropriate infrastructure equipment to enable measurements. In many cases, the planning and completion of experiments during the pre-project phase establish the project's scientific and technical feasibility, which are important determinants for deciding how to move the project further.

The PI needs to apply for a **PRC project** if the project requires extensive resources from CBCS. The purpose of the independent project review committee is to have a clear and transparent process where the allocation of CBCS resources is decided based on a combination of scientific impact and potential, and technical feasibility of ongoing and incoming project proposals. A more detailed description of the PRC process is described in section 4.3.

If the user needs less support and the project can be completed within 2 full-time equivalent weeks and it is scientifically sound, it is listed as a **Service project**. This is a decision made by each local node based on available resources. **Open access** services offered at the different nodes differ in extent and frequency. This can be a convenient alternative for the use of, e.g., specific plate readers, liquid handling robotics or microscopes. Depending on the level of operational difficulty, the user will be given an introduction and can then operate the instrument independently. Booking of instruments, availability and cost are set by each node.

An opportunity for the development of each infrastructure node is to engage in **Technical Development Projects.** With support from SciLifeLab, 20% of a CBCS staff position can be devoted to developing specific techniques, assays, etc.

EU-OPENSCREEN projects. KI and Umu are partner sites in the ERIC EU-OPENSCREEN and may provide both assay development and screening and chemistry support to projects entering through EU-OPENSCREEN. These projects are full cost coverage and as a partner site you have the possibility to offer your availability to support the user project through the EU-OPENSCREEN central office. The partner site provides a cost estimate for the project of interest and the user chooses which European site to collaborate with.

1.3 PRC PROCESS

1.3.1 PRC member composition

CBCS strives for all extensive projects to go through the PRC process to ensure that CBCS resources are put on the most scientifically promising and technically feasible projects. The project review committee is selected to consist of members with different expertise within biology, chemistry, drug discovery, and the pharmaceutical industry. At present, the PRC consists of Lena Ripa (AstraZeneca Mölndal), Samuel Svensson (Linköping University), Susanna Brighenti (Karolinska Institutet), Anja Sandström (Uppsala University), Martin Johansson (Aqillion) and Lars Svensson (Lund University Innovation). A CBCS staff member is assigned as secretary of the committee. The committee will be expanded to include 1-2 more members, considering the increase in applying projects we foresee with the expansion of CBCS nodes and capabilities.

1.3.2 PRC application template and its timelines

The application for a PRC project follows a template that has been in place since the initiation of the PRC process in November 2011. Since then, it has been revised several times, and we foresee that new revisions will be continuously released as the evaluation and review process is refined. The template serves to ensure all adequate aspects of the project proposal are covered, including:

- novelty of the proposal
- biological background and rationale
- the technical status and feasibility
- examples of known small molecule-based modulators
- funding status
- intended deliverables both from CBCS and from the PI´s group.
- a description of available downstream methods for further characterization of any molecules identified and/or synthesized during the project.
- status of downstream methods, such as availability in lab, resources, and funding to run them.
- publication plans
- relevant references

The routines for applying are as follows:

1. When the call for projects opens in the *SciLifeLab Anubis* portal, the applicant is informed to contact CBCS personnel well in advance of the application deadline. Applicants that have not completed this contact two weeks before the deadline will not be considered. However, we strive to contact presumptive users well in advance through outreach activities and webinars throughout the year.

2. Before the application deadline, CBCS personnel will guide the applicant to provide all requested information. In-depth discussions of the project improve our ability to judge the project's technical feasibility and enhance the user's understanding of the infrastructure's capabilities and limitations. Information about the cost model is also given to ensure the applicant will refrain from withdrawing interest after the PRC review process because of potential cost issues.
3. The applications to CBCS are submitted through the Anubis portal. The applicant fills in metadata, and the proposal is uploaded as a PDF file.
4. Upon closure of the call, two PRC members and one CBCS staff member are assigned to each proposal for in-depth review according to a template (described in section 4.3.3).
5. Each reviewer uploads their assessment to the portal. The evaluations become available to the PRC members once their assessments are submitted to ensure they remain unbiased.

1.3.3 PRC member preparations and evaluation criteria

The PRC members can access the submitted applications four weeks before the meeting at which the project priorities are determined. Given this material's sensitive character, the distribution is made through Anubis. The project applications and related information provided during the review process are confidential and are treated as such by the reviewers. Information within the documents is provided solely to evaluate the application and is not to be released or reproduced by anyone else. After completing the evaluations, any paper copies must be destroyed or returned to CBCS, and electronic documents must be deleted.

The applications are split between the PRC members such that each committee member is responsible for an in-depth review of their share of the applications. Each application is reviewed in this manner by two PRC delegates. The work is done independently, and PRC members cannot discuss the proposals between them at this point. The review is prepared separately for each project, with the evaluation criteria described below.

The PRC members´ evaluations focus on the biological rationale and scientific impact. In contrast, CBCS evaluations focus on technical feasibility and the prevalence of small molecules already described in relation to the proposal. This highlights whether a screen or the use of chemistry efforts is motivated or should the applicant instead be directed to already available tools when addressing the biological question.

PRC committee (scores from 1 to 5, where 1 = poor and 5 = excellent):

1. Biological rationale and potential scientific impact
    a. Research/technological quality with comments.
    b. Novelty and originality with comments.
    c. Relevance with comments.
    d. Overall score with comments.
2. Importance of CBCS efforts
3. Availability of described assays, resources, and funding, including follow-up and validation studies.
4. Scoring of publication plans

CBCS:

1. Is the requested work from CBCS feasible?

2. How many estimated full-time months of work from CBCS?
3. Are there already small molecules available?
4. List secondary assays suggested.
5. Monitor national spread and gender perspective.

For each aspect, relevant comments are made, and a score is given, which runs from 1 to 5.

1.3.4 PRC meeting routines

The meeting begins with a presentation of the portfolio status and progress made in existing projects by the node leaders or delegated personnel. The meeting will then follow a generic agenda as outlined below:

1. Portfolio and overview of progress — Responsible: Node leaders
2. Collection of and summary of reviews — Responsible: Secretary
3. Individual discussion of each proposal — Responsible: Assigned PRC members.
4. Summary and alignment of priorities — Responsible: PRC members

The collection and summary of individual reviews (point 2) enable a judgment of the consistency of assessments made by PRC members and CBCS personnel. In the next step, the PRC members will review the detailed evaluation made for each proposal they were assigned to and discuss the consistency of the assessments made for each. This discussion resolves any discrepancies in the views between PRC members and CBCS personnel. The CBCS secretary has booked telephone availability with the assigned CBCS personnel according to the pre-distributed agenda if that support should be required. At the end of the discussion, a priority score is given to the discussed proposal. The secretary documents the process. Finally, when all applications have been handled, the members of the PRC will be responsible for a discussion in which the balance of priorities between the projects is assessed.

It should be noted that these discussions are confidential, meaning neither the PRC members nor the secretary can discuss the contents of this evaluation process with others. Any potential questions on this matter should be directed directly to the chair.

The PRC will also consider re-prioritization of ongoing CBCS resources if insufficient resources exist to accommodate all projects.

1.3.5 Meeting notes and implementation

The secretary distributes draft meeting notes from the meeting, including the finalized scoring of the proposals, to the PRC members, who subsequently review them for completeness and correctness. Any additions and corrections are returned to the secretary. The finalized protocol is then prepared and placed on the file server available for the PRC representatives. The protocol is also distributed to the node leaders, who will plan resources based on the project scores. The planning is then decided on in the next CBCS steering group meeting, which resolves any discrepancies or issues regarding the project priorities. The applicants are further contacted and receive the PRC comments, priority, and an assigned CBCS contact person.

2 PROJECT MANAGEMENT ROUTINES

2.1 PROJECT ONBOARDING

The first step in project onboarding is the establishment of a project agreement/user rules between the applicant and CBCS. This includes project-specific details, such as an experimental plan, timelines and cost estimates based on the applicable cost model. Identification of stop/go points, and associated timelines are critical at this point to ensure optimal usage of CBCS resources. In some cases, the PRC has specified additional criteria for running the project, that need to be taken into consideration. The CBCS user agreement also stipulates conditions for publication of results in accordance with scientific praxis and the SRC's open access rules.

The user agreement includes a section on intellectual property rights. In general, CBCS encourages users to continue promising projects with potential commercialisation value in e.g., local biotech incubators. In general, the CBCS staff release intellectual property rights to the user. Once the user agreement is established, practical work will begin.

2.2 PROJECT EXECUTION

Each project is assigned a biologist and a chemist that are present at different steps of the project. A typical project flow is outlined in Figure 4. The projects are also discussed at designated project meetings once a month, that ensures that the broad expertise present in CBCS is utilized and drives the project forward.

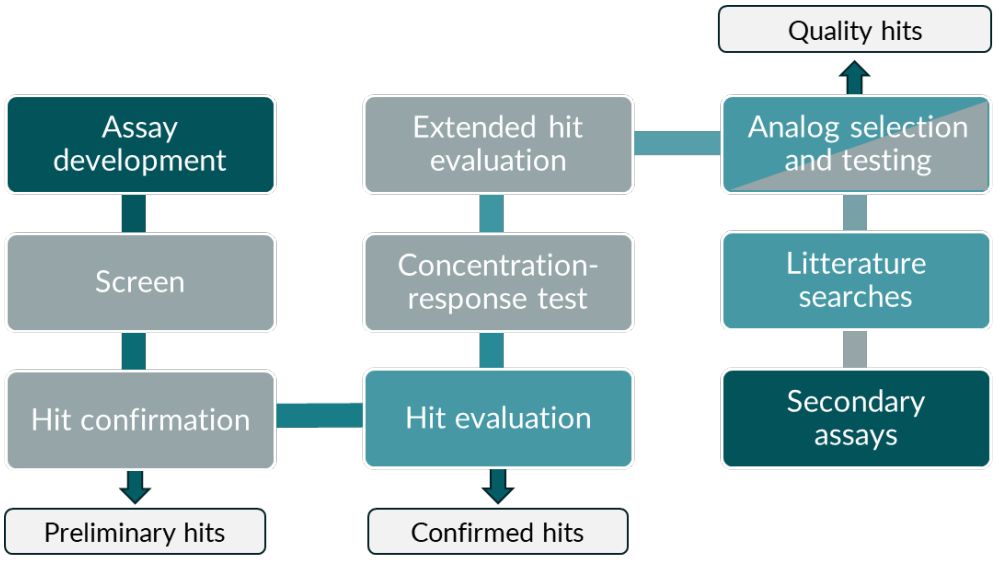

Figure 4. A typical workflow of an assay development and screening project at CBCS. The different colors indicate the main responsible part. Dark green: PI, Grey: Biologist, Aqua: Chemist.

2.3 PROJECT COMPLETION

The CBCS project manager will provide a final report when a project is completed. The report minimally contains all necessary data, figures, and experimental details for publication. The report also includes how data is stored and delivered to the user. Detailed materials and methods descriptions are encouraged and stored in secure shared folders (see section 6, data management). In addition, all primary data generated by CBCS is delivered to the PI at this time and the report includes

detailed information on how data has been stored in accordance with the agreed upon DMP. The CBCS project manager then changes the status of the project to complete in the project database.

CBCS encourages PIs to publish papers on the results coming from their projects, when possible. CBCS funders demand that users of the infrastructure publish results as open access (free-of-charge online access for any user). CBCS requires staff scientists to apply their ORCIDs (Open Research and Contributor Identifiers) to all publications and data depositions where possible and users to acknowledge CBCS.

2.4 CONFLICT RESOLUTION

When more than one user approaches CBCS with a project proposal addressing the same targets or project goals, CBCS has established the following procedures: if there is an overlap during the consultancy meeting CBCS stops the discussions and informs the second user about the situation. CBCS proposes to mediate an interaction between the two users. In the case that there is mutual interest to discuss a collaboration the users can move forward together with a joint project with CBCS. CBSC will not screen the same compound collection on the same target for different users unless explicit biological differences are expected. If a PRC member is a co-applicant or applicant of a project, they inform CBCS two months prior to the application deadline and will excuse themselves from the evaluation process. The remainder of the PRC members will evaluate the application.