Framework for Handling PSI-2 Community Nominated Targets

The PSI mission includes interaction with the general community to aid characterization and structure determination of community nominated targets. Many interactions and collaborations have already been established with the community by the individual PSI production centers and specialized centers and are already contributing to this end. However, it is appreciated that a more formal and transparent mechanism should be established to coordinate, review and arbitrate on targets proposed by the community. An independent review panel, the PSI Community Target Committee, will be established to review such proposals in much the same way that proposals are reviewed at synchrotrons for communal beam time. The committee will consist of nominated representatives from each of the 4 production centers, one acting for the specialized centers one from NIGMS, and 2-3 from the community. It is important to establish some ground rules for submission and selection of targets in order to provide maximal impact to the community, as well as to increase the likelihood of success. The following guidelines are currently proposed and these will be modified, if necessary, on a semiannual basis to optimize and streamline the process:

- Targets that are nominated by the community should be consistent with the overall mission of the <u>PSI</u>. Priority will be granted to novel targets with less than 30% identity to any other structure deposited in the <u>PDB</u>. Ideally, nominated protein targets would also meet goals for high novel leverage, such as representing first structures from large sequence families or modeling families. High value targets, such as membrane proteins, protein-protein complexes, and eukaryotic proteins may also be considered, but these may be more appropriate for the specialized centers.
- 2. It is expected that all coordinates for nominated targets, including any nominations from for-profit organizations, will be deposited in a timely manner and be subject to the same regulations that the PSI enforces on its own centers for deposition and release of coordinates (i.e. less than one month from completion of the structure, see <u>Policy on Release of Structures</u>). It is also expected that all clones leading to successful structures will be deposited in the <u>PSI Materials Repository</u>. It is also expected that the investigators submitting such nominations will make every effort to submit publications based on the PSI work, either in consultation with or in collaboration with the PSI center, as appropriate.
- 3. When targets are proposed, a rationale for why these targets should be studied must be briefly outlined, and whether any previous work has been performed on these targets. It is important to provide full sequence information, as well as any constructs that have been attempted for protein production and/or crystallization. Recommendations as to whether this would be a target for a production center or a specialized center would also be useful, and whether X-ray or NMR is more suitable. It may be prudent to contact one of the centers for guidance before submission especially if there are any questions, particularly about general feasibility or appropriate methodologies. Foreign investigators are encouraged to consult with the PSI Center Director prior to submitting nominations.

- 4. It is important that any targets that are taken on by the PSI have at least the same chance of success as the targets that are already in the overall pipelines of communal targets chosen by the PSI itself. The goal is to provide useful structures to the community with a reasonable success rate, so that the PSI can contribute substantially to the community efforts.
- 5. Targets which would not normally be within the mission of the PSI would be those that have high sequence identity to other targets in the PDB and structure determination of complexes of known targets. Exceptions could be made in some instances for particularly high value targets for which it has been difficult to achieve success despite the high sequence homology to known structures, and complexes between proteins of known structure with proteins of unknown structure, or for those of exceptionally high biomedical relevance.
- 6. If protein samples are provided by the community, then the protocols used for sample production must be well documented and would normally include expression system, purity, stability, buffers and whether the protein can be concentrated to at least 5-10 mg/ml for crystallization studies. Similar sets of feasibility criteria, including demonstration of sample stability and high quality HSQC spectra, would pertain to targets proposed for NMR study.
- 7. The PSI Community Target Committee will review these proposals and make recommendations to the PSI as to the value of the target, the feasibility of success, and whether it is within the stated mission of the PSI. The review committee should decline targets that are not well thought out or for which there is not the likelihood of substantial biological follow up studies from the investigators that are making the proposal. Recommendations by the committee may also include suggestions for which PSI technologies or methodologies could be applied to the targets in question by the investigators themselves. In this way, such PSI methodologies can be rapidly transferred to the community and applied to other protein targets in their own laboratories.
- 8. The review committee will review targets electronically once per month depending on demand, but less frequently if there are insufficient proposals to review, and make recommendations within a week of the committee review. It is not intended that a formal meeting of the committee take place, but the review process could be similar to review processes that are already in place at synchrotrons where electronic reviews can be submitted.
- 9. Once the proposals are accepted, each PSI center handling the proposal will nominate a contact person that will interface both with the review committee and the community investigator. It is critical that the community investigator also nominate a contact person to ensure easy communication and flow of information.
- 10. Proposal forms can be accessed on line from the PSI Knowledgebase (<u>http://kb.psi-structuralgenomics.org</u>) and the proposal will be submitted to a secure KB Web site. The review committee will access proposals electronically from this site and the reviews will also be archived there. Proposals and reviews will be available to the review committee members and the PSI Center Directors.

11. Dr. Ward Smith, NIGMS (smithwar@nigms.nih.gov) will chair the review committee, notify the investigators within six weeks as to the decision by the reviewers, and answer any questions on the process from the community. Any comments and suggestions should be addressed to Dr. Smith.

POLICY AS OF JUNE 8, 2009