# Eli Lilly and Company

# LRL-CAT

**(Lilly Research Laboratories – Collaborative Access Team)**

# EXPRESS CRYSTALLOGRAPHY PROGRAM

## Policies and Procedures

https://lrlcat.lilly.com

us_lrlcat_guinfo@lilly.com

### LRL-CAT Staff

| | | | |
|---|---|---|---|
| Jordi Benach | Sr. Director - Chemistry &<br>Head of LRL-CAT Operations | 630-252-0821 | benach_jordi@lilly.com |
| Anton Frommelt | Principal Engineer | 630-252-0827 | frommelt_anton_joseph@lilly.com |
| Chi Young Moon | Research & Development Consultant | 630-252-0822 | chiyoung_moon@network.lilly.com |
| Laura Morisco | Associate Director-Operations | 630-252-0824 | Morisco_laura@lilly.com |

**LRL-CAT | Advanced Photon Source | Argonne National Laboratory**
**9700 S. Cass Avenue | Building 438A | Sector 31 | Lemont, IL 60439**

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# 1. Overview

LRL-CAT offers "Express Crystallography", an **UNSCHEDULED**, **FULL-SERVICE**, **MAIL-IN** protein crystallography service, to industrial, government, and academic Users of the Advanced Photon Source. Through this program, researchers can obtain data from a highly efficient and automated X-ray beamline based on specifications from the program's participants.

All Proprietary requests will require contract agreements. LRL-CAT offers a Fee for Service or Long-Term Program. For program details, contact us at:
us_lrlcat_guinfo@lilly.com

All Non-Proprietary requests for data collection at LRL-CAT are managed as rapid access proposals through the General User Program of the Advanced Photon Source. Proposals may be sent to the APS at any time. Once a proposal has been submitted and all safety documentation provided and approved by the APS and LRL-CAT, samples can be run quickly when the APS is operational. The turnaround for screening images and datasets is within 1-2 days. Although usually, Users get their data within 24-32 hours of shipment.

# 2. Getting Started

## 2.1. Review LRL-CAT Technical Capabilities

Before submitting a proposal, prospective Users should review the technical capabilities and specifications of LRL-CAT. This review will ensure that the beamline facilities meet the User's requirements and that all needed equipment and instrumentation are available. The LRL-CAT technical specifications are as follows:

- Technique: Macromolecular crystallography.
- Insertion Device: Undulator A (3.3 cm period)
- Monochromator: HLD-15 Double Crystal $LN_2$ Cryocooled (KOHZU).
- Crystals: Silicon (111).
- Energy range (beamline, standard configuration): 5.0 – 22 keV (0.56 – 2.47 Å).
- Energy resolution: ~0.01 % (FWHM).
- Focused beam size (H x V) (FWHM): ~40 µm x 40 µm (sample position). Maximum focus ~7.4 µm x 2 µm (commissioning phase).
- Flux at sample position (Se K edge, $3^{rd}$ harmonic of undulator): ~7 x $10^{12}$ (photons / second, measured with calibrated Si pin diode, and ~200 mA in the APS storage ring).
- Detector: Pilatus3 S 6M (DECTRIS)**:** Maximum frame rate 25 images / second.
- Robotic Sample Changer: ISARA (IRELEC).

- Robotic Sample Changer maximum capacity: 464 crystals.
- Crystal centering: Automated loop and X-ray (raster), and manual.
- Crystal Base: SPINE (Molecular Dimensions).
- Crystal Loops: Hampton Research standard nylon loops.
- Beamline Control Systems: Python, C, EPICS, spec on Linux.

## 2.2. Review Procedures for LRL-CAT Express Crystallography Program

LRL-CAT has a highly automated system for tracking samples and collecting data. The instructions must be followed in detail to maximize the quality of your results and smoothness of the whole procedure. (See Section 3).

**Proprietary Users can skip to Section 3.**

## 2.3. Acceptance of Requirements for Participating in the LRL-CAT General User Program

SUBMISSION TO THE APS OF A GENERAL USER PROPOSAL FOR LRL-CAT CONSTITUTES ACCEPTANCE OF THE CONDITIONS AND PROCEDURES LISTED IN APPENDIX A.

## 2.4. Submit General User Proposal to the APS

Submission of a General User Proposal at LRL-CAT is coordinated through the APS General User System. In most cases, beamtime will be allocated and data collected before your General User Proposal is reviewed by the APS.

The APS provides information on access procedures via its online proposal system (see https://www.aps.anl.gov/Users-Information/Getting-Started/User-Checklist). Users can create, edit, and view proposals or request additional time for existing proposals. All beamtime requests at LRL-CAT 31-ID-D must be submitted as "mail-in" Rapid Access proposals.

As part of the proposal, the User includes a request for shifts of 8 hours. Users can estimate the number of shifts based on the following statistics: LRL-CAT can screen approximately 43 crystals per hour. A typical diffraction dataset of 180 ° (900 frames at 0.2 degree / frame and 0.1 second / frame exposure) requires ~2.9 minutes. Therefore, for standard crystals, LRL-CAT can collect ~18 datasets per hour, which includes crystal mounting, centering, and dataset collection. When X-ray centering is needed, LRL-CAT can collect ~8-10 datasets per hour. For well-diffracting crystals and only loop centering, LRL-CAT can collect up to 30-40 datasets per hour.

Each proposal is also required to have a current APS Experimental Safety Assessment Form (ESAF). The ESAF must be completed and approved by both the Advanced Photon Source and LRL-CAT prior to shipment of the Dewar containing the User's samples.

# 3. LRL-CAT Express Crystallography Procedures

## 3.1. Contact Information

Each User will be assigned a unique contact identification number (Contact ID) that will be used for correspondence with LRL-CAT. Users only need to request a Contact ID during their first experiment at LRL-CAT. The identity of the User should be linked to the Principal Investigator. See Section 5 below for the Contact ID request form and information to be submitted to LRL-CAT.

## 3.2. Sample Preparation

The LRL-CAT Express Crystallography Program relies on procedures for sample preparation and documentation that have been used at the beamline since the beginning of 2004. These procedures are designed to maximize the efficiency of beamtime utilization at LRL-CAT and the quality of communication between the Users and LRL-CAT personnel. Users are strongly encouraged to follow the sample preparation instructions to the letter.

### 3.2.1. Obtain Barcoded Bases

All pins must be mounted in Molecular Dimension bases which are compatible with the IRELEC ISARA cryo-sample changer (robot) in use at LRL-CAT. Order the Molecular Dimensions Cryo-caps with Data-Matrix (MD7-401) or without (MD7-400). Hampton or MiTeGen bases are NOT compatible with our robot.

### 3.2.2. Use 18 mm Pins

The pins attached to the bases must be 18 mm in length. Mounted cryo-loops (constructed from nylon fiber whose diameter is ~20-100 microns) from Hampton are ideal for this purpose. The pins are scored to permit the creation of different lengths. Break the pin at the second score from the non-loop end to yield a pin that is 18 mm long.

Do NOT use loops whose fiber is 10 microns in diameter. These loops lack enough visual contrast to be recognized by the LRL-CAT automated loop-centering software. **Litho-type loops (such as those from MiTeGen and Molecular Dimensions) are NOT compatible with our automated centering system.**

Be sure to glue the pin firmly into the base. In our experience, Super Glue or equivalent works best. Epoxies do work but require greater care. If the pin is not held firmly to base, the crystal may not remain in the X-ray beam during your experiment and/or may cause a robot crash (and subsequent loss of sample) during mounting/unmounting of the sample.

Any deviation from these rules will cause delays on beamline operations, delay data turnaround, and increase workload on beamline staff.

### 3.2.3. Obtain 1D Barcode Labels from LRL-CAT

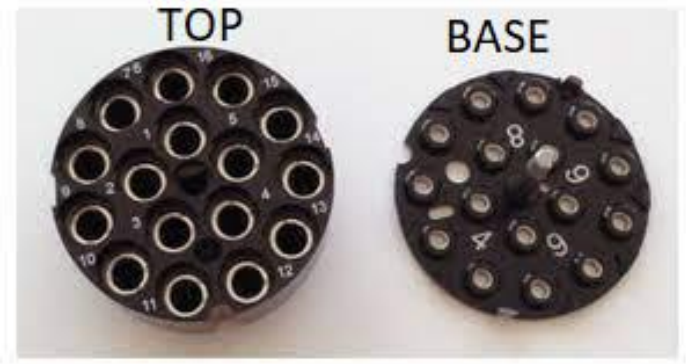
LRL-CAT tracks all samples with a 2-barcode system:

- One 2-inch 1-D barcode that represents the primary crystal identifier.

- One 1-inch 1-D barcode that identifies the puck.

1. **The (2-inch) barcode label NUMBER is to be entered into the spreadsheet to identify the samples.**
    - Dispose of the actual label once you have entered the unique barcode number in your spreadsheet.
    - You may adhere the label to your notebook for data keeping purposes only.

The (1-inch) barcodes should be adhered to the puck. Do not attach any other labels to the puck. Do not reuse barcode labels.




LRL-CAT will either mail the barcodes to the Users or ship them via Federal Express® if the User provides LRL–CAT with a FedEx account number.

The UniPucks should have unique codes etched on the side of the top and at the bottom of the base. This etched code should be either entered in the Notes section of the User spreadsheet or recorded by the user. This is in case the 1-inch barcodes provided by LRL-CAT fall off during Dewar transport.

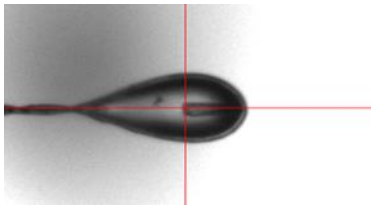
### 3.2.4. Crystal Mounting

LRL-CAT will auto-center all samples in the X-ray beam using a robust, proprietary loop-centering algorithm developed by LRL-CAT. This algorithm requires that the submitted crystals be placed into loops that are commensurate with crystal size. The auto-centering system detects the cryo-loop within a video image of the loop. It does not attempt to find the crystal.

If the beamline staff notices that the crystals are not centered in the loop or if the location of the crystal inside the loop cannot be properly seen, beamline staff will proceed to center the crystal using X-rays (raster). Beamline staff then marks these samples for automated raster centering, and a raster centering step is performed before screening and/or data collections are conducted.

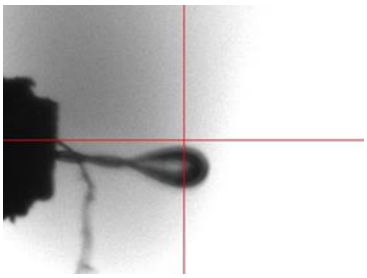
Currently, the fully focused beam size at LRL-CAT is approximately 130 x 50 $\mu m^2$ (H x V) (FWHM) at sample position and the standard energy of ~12.66 keV (Se K edge). Therefore, loops with a maximum dimension of ~70 microns have the best chance of being centered correctly. If the crystal is significantly smaller than the loop or is not

centered within the loop (see following picture), it is possible that the crystal will not be in the beam during data collection. Beamline staff will try to resolve this issue manually before it happens either by marking the crystal for manual centering and/or X-ray raster.

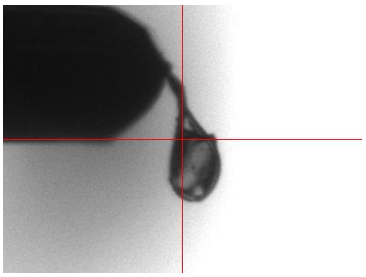


The automated loop-centering system is extremely sensitive to anything that is not a loop, please try to avoid:

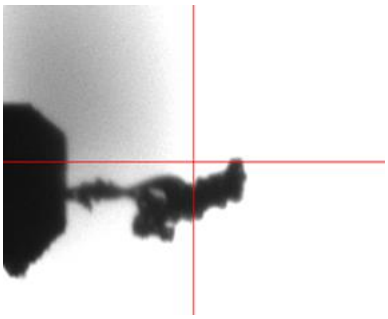
- Extra threads/fibers on the loop, crystal or pin:



- Loops that are too bent:



- Ice/frost on the loop/sample or pin:



Any deviation from these rules will cause our auto-centering program to fail and beamline staff will have to center the samples manually re-screened them and if they reach the resolution cut-off manually collect a dataset from them, thus delaying data turnaround and increase workload on beamline staff.

### 3.2.5. Pucks

Samples will be shipped to the beamline already loaded in UniPucks. In order for the new data collection process to be as robust and user-compatible as possible, LRL-CAT is now only using UniPucks. These pucks are available from MiTeGen & Molecular Dimensions. They also come as part of a starter kits which contain the essential tools necessary for UniPuck storage, handling, and shipment. To avoid any issues, each UniPuck should have a unique code etched or engraved on them (usually offered free-of-charge by the vendors).

- MiTeGen, UniPuck Starter Kit: (SKU) M-CP-UPSK001
- Molecular Dimension, UniPuck Starter Kit: MD7-600

### 3.2.6. Dewars

The diameter of the interior of the Dewar must match that of the shelved UniPuck shipping canes. The Taylor-Wharton standard dry shipper (CX100B-11M) is compatible with the EMBL equipment. Some Dewars currently used to ship crystals have diameters that are too small to accept the shelved UniPuck shipping canes.

### 3.2.7. Data Transfer

LRL-CAT provides direct transfer of data to the User through the internet. This approach will deliver data seamlessly to the User as soon as screening images and individual datasets are collected and processed. Data will appear as a zipped tar archive (*.tar.gz) that will include all images and processing files. There are two ways we can deliver the data to the User:

1) Data can be transferred to our sftp server for the User to retrieve:

For this, an sftp account will be created in our sftp server or, for existing accounts, the account will be re-activated and the password changed.

New login information is sent securely to the User usually the day the beamline staff receives the spreadsheet or during the data collection day.

Passwords and access to the sftp account expire after 14 days.

2) Data can be transferred to a User's sftp server.

In this case, we need the following information:

- server DNS name or IP address (required)
- username (required)
- password (required)
- server path (optional)

Please contact us for additional help:

Jordi Benach (benach_jordi@lilly.com)
Anton Frommelt (frommelt_anton_joseph@lilly.com)

## 3.3. Sample Documentation

### 3.3.1. Standard Data Collection Conditions

The Default Data Collection Parameters used at LRL-CAT are:

Crystal screening:

- X-ray Energy: Selenium K absorption Edge (12660.3 eV)
- Exposure: 0.48 seconds
- Oscillation: 1 degree
- Total Number of frames: 4
- Starting angles (degree): 0, 45, 90, 135

Dataset collections:

- X-ray Energy: Selenium K absorption Edge (12660.3 eV)
- Exposure: 0.1 seconds
- Oscillation: 0.2 °
- Total Number of frames: 900 (1800)
- Total angle oscillation: 180 ° (360 °)

If no space group information is available and the indexing of the screening images shows the possibility for P1 as space group, then 360 ° of data are collected automatically. This is done by collecting 1800 frames at 0.2 ° per frame and 0.1 seconds per frame.

Nonetheless, the User can specify any range of total oscillation angle, number of frames, frame oscillation, exposure, or energy (see Excel® Sample Submission Spreadsheet instructions in the next section).

The exposure/transmission will be reduced by the beamline staff for crystals that are clearly sensitive to radiation damage. If the User has previous experience/knowledge about the radiation sensitivity of the crystals, please let the beamline staff know about it via the comments section in the Excel® Sample Submission Spreadsheet (see next section).

### 3.3.2. Instructions for Sample Submission Spreadsheet

Diffraction screening images and datasets are collected according to the Default Data Collection Parameters (previous section) or by the instructions provided by the User.

These instructions are communicated to LRL-CAT through an Excel® Sample Submission Spreadsheet. The contents of this spreadsheet are loaded directly into the sample management database used by LRL-CAT. This procedure ensures the greatest accuracy in communication with beamline personnel. For this reason, it is imperative that all information in the spreadsheet be correct.

To request a copy of the Sample Submission Spreadsheet, please send an email to us_lrlcat_gusamples@lilly.com. Once complete, the spreadsheet should be emailed to the same address.

#### 3.3.2.1. Rename the Spreadsheet

The form of the name should be a combination of your last name, first initial, contact ID, the current date, and the standard extension for an Excel spreadsheet, ".xls". The format for the date is YYYYMMDD. For each spreadsheet submitted, please append "_n" (n = 1, 2, 3...), which will differentiate the files when more than one spreadsheet is provided. The proper form for the file name is as follows: "Doe_J_10_20100930_1.xls".

#### 3.3.2.2. Enter Information in the Spreadsheet

These instructions refer to specific cells in the spreadsheet.

No special characters, such as – (hyphen), ?, >, <, () (parentheses), etc. may appear anywhere in the spreadsheet. When there is a choice of two values, for example when a specific protein construct crystallizes in two different space groups, enter only the most likely value. If a specific datum is unknown, leave the cell blank.

Only integer or real values are permitted for numeric values. Any restrictions are logical. For example, the number of frames must be an integer while the oscillation angle can be real or integer.

Some examples for entries are enclosed in quotation marks. Do not include these marks in the actual spreadsheet.

Each entry is listed as required, default, or optional. Those with default values will take those values if alternatives are not specified by the User. However, it is best to fill in the values, even when they are the same as the defaults, to ensure that LRL-CAT examines the crystals as the User desires.

#### 3.3.2.3. Contact ID (cell B5) – Required

In cell B5 enter your permanent contact identification number. This number was assigned through the Contact ID request form the first time you submitted samples to LRL-CAT. The contact ID is your primary identification for the LRL-CAT Express Crystallography Program.

#### 3.3.2.4. Name & Email (cells B7, D7 & B9) – Required

In cell B7 enter your first name. In cell D7 enter your last name. Be sure to use the same names each time you fill out this spreadsheet. Please use the legal form of your name (i.e. no nicknames). In cell B9 enter your email address. The email should be the same as that originally provided to LRL-CAT. Your name and email are used as a secondary verification after the Contact ID. If your name and/or email have changed, please update

this information by communicating with us_lrlcat_guinfo@lilly.com before submitting the spreadsheet.

#### 3.3.2.5. GUP, BTR, & ESAF (cell B12, D12, & F12) – Required for Non-Proprietary Users only

In cell B12 enter your 5-digit General User Proposal (GUP) number. In cell D12 enter your 6-digit Beam Time Request (BTR) number. In cell F12 enter your 6-digit Experiment Safety Approval Form (ESAF) number.

#### 3.3.2.6. Crystal Information

Beginning in row 18, enter the information for each crystal. These instructions describe a single crystal on row 18. For each subsequent crystal, use the following rows. Single blank rows between groups of related crystals or canes are permitted. Do not leave 2 or more consecutive empty rows.

#### 3.3.2.7. Puck Barcode Label (cell A18) – Required

In cell A18 enter the barcode that has been placed on the exterior of the puck. The entry here must exactly match that on the barcode. Capitalize all letters, include all zeros, and do not add any spaces. (Example: APS12345)

#### 3.3.2.8. Puck Position (cell B18) - Required

In cell B18 enter the sample position in the puck. Puck positions are labeled 1 through 16. Each UniPuck holds up to 16 samples.

#### 3.3.2.9. Sample Barcode (cell C18) – Required

In cell C18 enter the barcode to identify your sample. Capitalize all letters, include all zeros and do not add any spaces. (Example: APS98765) Record the sample barcode numbers in your notebooks after use by either writing down the ones already used, or simply discard the labels.

#### 3.3.2.10. Group Sample Barcode (cell D18) - Required

In cell D18 enter the group sample barcode. This cell is used to identify equivalent or duplicate crystals. Choose one sample barcode from an equivalent set of crystals and enter it as the group sample barcode for all the crystals within the set. When testing cryo-protectants, it makes sense to group crystals with similar protectants together. The same is true for crystals nominally identical in preparation. However, it is often appropriate to group different soaking conditions for ligands separately.

#### 3.3.2.11. Cap 2-D Barcode (cell E18) – Optional

In cell E18 enter the printed (not glued) 2-D barcode located on the side of the base (optional). PLEASE DO NOT WRITE ON THE BASE OF THE CAPS.

#### 3.3.2.12. Number Group Datasets (cell F18) - Required

In cell F18 enter the integer number of datasets to be collected from the group. If the cell is blank, a value of 1 is assumed. Beamline staff will collect additional crystals of the same group if they may reach the resolution cut-off (but were not selected automatically by the beamline software). Users can also ask beamline staff to collect or re-collect any

additional crystal. This is to ensure that the User gets the best data from each batch of crystals.

#### 3.3.2.13. Protein (cell G18) – Required

In cell G18 enter a descriptive name for your protein. This name will be used for any direct communication between LRL-CAT personnel and the User. Do not use spaces, parentheses, hyphens, forward slashes or back slashes in the name.

Underscores (_) may be used in place of these characters**.** The maximum length for protein name is 25 characters.

#### 3.3.2.14. Ligand (cell H18) – Optional

In cell H18 enter the name of any ligand. As in the protein name, use underscores of non-alphanumeric characters. The ligand will appear in the name of the dataset. If no ligand is provided, dataset names will include the term "NONE". The maximum length for ligand name is 25 characters.

#### 3.3.2.15. Space Group (cell I18) – Required if known

Enter the space group in cell I18. Leave the cell blank if the space group is not known or the User is not completely sure about it.

Use the Hermann-Mauguin notation: Use capital letters. Do not use subscripts or parentheses. Example: use P212121 **instead of** P2(1)2(1)2(1) or P 21 21 21.

#### 3.3.2.16. Unit Cell (cells J18 to O18) – Required if known

In cells J18 to O18 enter the unit cell dimensions and angles (a, b, c, alpha, beta, gamma), if known. Leave all these cells blank if one or more dimensions are unknown. Units are angstroms and degrees. Do not include the units in the cells.

#### 3.3.2.17. Mosaicity (cell P18) – Optional

Enter the estimated mosaicity in cell P18, if known. Otherwise, leave blank.

#### 3.3.2.18. Cut-off Resolution (cell Q18) - Required

In cell Q18 enter the minimum acceptable resolution for data collection. If the crystal diffraction does not reach this resolution, the crystal will not be automatically selected for dataset collection. However, beamline staff may override the beamline software and re-/collect additional promising crystals.

#### 3.3.2.19. Detector Resolution (cell R18) – Do Not Use

Leave cell R18 blank.

#### 3.3.2.20. Single Wavelength (cell S18) - Required (if anomalous element is not present)

In cell S18 enter "Yes" or "Y" if the crystal does not contain an anomalous element. All single wavelength collections will be done at the Selenium K edge (i.e. 12.66 keV). However, an affirmative answer here indicates that an alternative wavelength of similar X-ray energy may be used.

#### 3.3.2.21. Anomalous Element (cell T18) - Required (if anomalous element is present)

In cell T18 enter the symbol from the periodic table of elements for the anomalous element present. For example, if the anomalous element is Platinum, enter "Pt". For mercury, enter "Hg". DO NOT SPELL OUT THE NAME OF THE ELEMENT. Do not include quotation marks in the cell. Use standard chemical symbol notation: "Pt ", not "PT". If an anomalous element is not present or is not to be used in determining the appropriate X-ray energy, LEAVE THIS CELL BLANK.

When more than one potential element is present, such as with tantalum bromide, the User must choose only one element for the anomalous scatterer. Any additional potential anomalous scatterer can just be noted in the comments section. Experience at LRL-CAT indicates that crystal radiation damage may prevent collection of diffraction data at two different X-ray wavelengths from the same crystal.

#### 3.3.2.22. Peak (cell U18) - Required (if anomalous element is present)

If an anomalous element is present and listed in cell T18, "Yes" or "Y" should be entered here. For single wavelength samples, this cell should be left blank.

The requested measurement for a single crystal must be either a single wavelength or anomalous experiment. Therefore, only one of cells S18 (single wavelength) and cell U18 (peak) should be answered in the affirmative. LRL-CAT staff will use their best judgment if there is any ambiguity within these entries.

#### 3.3.2.23. Remote (cell V18) - Optional (only if anomalous element is present)

If a dataset at a remote energy is required, enter "Yes". Otherwise enter "No" or leave blank. The remote energy will usually be 200 eV above or below the absorption edge of the anomalous element. Note, that LRL-CAT uses SAD almost exclusively for anomalous experiments and encourages Users to do the same.

#### 3.3.2.24. Oscillation (cell W18) – Default

In cell W18 enter the oscillation in angular degrees for a single image or frame. This value will be used for data collection. With our Pilatus 3 S 6M detector, thin-slicing or values between 0.1 - 0.3 ° are recommended to provide the best data. If the cell is blank, an oscillation of 0.2 ° will be used. The allowed entries are integer or real numbers. If the oscillation angle is entered, PLEASE also write the total number of frames (next section).

#### 3.3.2.25. Number of Frames (cell X18) - Default

In cell X18 enter the number of frames required for the dataset. The default number is 900 with an oscillation of 0.2 ° per frame. For most experiments, a data wedge of 180 ° (frames times oscillation) should be used.

- For crystals known to be triclinic (P1) or for anomalous data collections, 360 ° of data will be collected (1800 frames at 0.2 ° per frame).

- If the space group is not provided and the indexing of the screening images suggests a possible P1 space group solution, 360 ° of data are collected automatically.
- If only 180 ° have been collected and the final dataset symmetry turns out to be P1 after data analysis and processing, a second additional wedge of data (200 °) will be collected to increase completeness/multiplicity. This additional dataset can be then merged by the User with the first one to increase completeness/multiplicity.

#### 3.3.2.26. Maximum Exposure (cell Y18) – Optional

Generally, this cell is left blank. It communicates information on the stability of the sample, if known. Enter a real number.

Typical exposures at LRL-CAT are 0.1 second (at the Se K edge) or lower depending on energy/flux per 0.2 degree oscillation.

- For crystals that are known to be radiation sensitive, smaller exposure values should be used.
- LRL-CAT staff may reduce the exposure if obvious radiation damage is observed in equivalent crystals.
- The exposure will vary as well (usually shorter), if the energy is different to the standard Se K edge, as the flux at sample position varies significantly with energy.
- The minimum value is 0.04 seconds / frame.

#### 3.3.2.27. Priority (cell Z18) - Do Not Use

Leave cell Z18 blank.

#### 3.3.2.28. Notes (cell AA18) – Optional

Enter any comments here as text. Brief comments are best. The comment should be entered in this cell only. Although highly recommended, you have the option to enter the PUCK etched/engraved code in the NOTES column.

Critical data collection instructions should be communicated in the text of the email when sending the completed spreadsheet.

### 3.3.3. Safety Documentation

As noted in section 2.4, for General Users of the APS, a valid Experimental Safety Assessment Form (ESAF) is required. The ESAF must be completed and approved by both the Advanced Photon Source and LRL-CAT prior to shipment of the Dewar containing the User's samples.

Samples submitted to LRL-CAT must be at Biosafety Level 1 (BSL-1) or lower. See https://www.aps.anl.gov/Safety-and-Training/Safety/Experiment-Safety/Hazard-Classes for a description of APS requirements for BSL-1 materials.

## 3.4. Sample Shipment

### 3.4.1. Prepare Dewar for Shipping

The User should ship crystals to LRL-CAT in standard dry shippers. The diameter of the interior of the Dewar must match that of the shelved UniPuck shipping cane. The shippers (CX100B-11M) are available from Taylor-Wharton.

All shipments to LRL-CAT must comply with the regulations of the Department of Transportation (DOT), Department of Energy (DOE) and Argonne National Laboratory. Users are to follow APS procedures for dry shippers.

Shipments must be non-hazardous. Accordingly, LRL-CAT **does not** accept crystals that have been frozen in propane or any other hazardous materials. In order to comply with APS User Policies and Procedures for Hazmat Transport, **the User must remove all free-flowing liquid nitrogen prior to shipment.**

The APS and LRL-CAT require that conformance with safety policies, including those for shipments, be scrupulously observed. Therefore, the following paragraph must be read and understood by the User.

**USERS ARE PROHIBITED FROM SENDING ANY DEWAR(S) THAT, EITHER DUE TO THE PRESENCE OF FREE-FLOWING LIQUID NITROGEN OR OTHER MATERIALS, WOULD BE CONSIDERED A HAZARDOUS SHIPMENT BY ARGONNE NATIONAL LABORATORY, THE U.S. DEPARTMENT OF ENERGY, THE U.S. DEPARTMENT OF TRANSPORTATION, AND/OR THE INTERNATIONAL AIR TRANSPORT ASSOCIATION. LRL-CAT ASSUMES NO LIABILITY FOR HAZARDOUS SHIPMENTS FROM THE USER.**

LRL-CAT is expected to inform the safety officers of the APS and the User of the failure to comply with existing regulations. Non-compliant shipments will be managed as directed by the APS.

### 3.4.2. Shipping Address

Federal Express® and its drivers are familiar with shipping procedures at the APS. For this reason, LRL-CAT does not use other express carriers.

All shipments of crystals for the Express Crystallography Program are to be sent by Federal Express® to:

LRL-CAT
Advanced Photon Source
Argonne National Laboratory
9700 S. Cass Ave, Building 438A, Sector 31
Lemont, IL 60439

The receiving department of Argonne National Laboratory is closed on Saturday and Sunday, as well as most Federal Holidays and the week between December 25$^{th}$ and

January 1st. All shipments should be delivered to the APS during the normal work week (Monday through Friday). A shipment sent on Friday should be designated for Monday delivery.

#### 3.4.3. Notification of Dewar Shipment to LRL-CAT

After shipping, send the tracking information to us_lrlcat_guinfo@lilly.com. The tracking number is also to be included in the sample submission form.

## 3.5. Screening Results and Data Collection

Over the past several years, LRL-CAT has found that Users obtain the best data when collection decisions are made by the LRL-CAT staff. LRL-CAT examines around 10,000 crystals per year and our staff has an exceptional understanding of how to maximize the quality of your data collection. Screening images and collected datasets will be automatically transferred (sftp) and available to the User as they are generated and/or processed. The entire process is fast and seamless for the User.

## 3.6. Return of Samples and Data

### 3.6.1. Data and Dewar Returned to User

The crystals will be returned in the original Dewar. The cost for shipping the Dewar will be charged to the User's account with Federal Express®.

### 3.6.2. Deletion of Collected Data

In order to ensure that the User's information is available solely to the User, all screening images and datasets will be deleted from LRL-CAT computers 7 days after the data have been successfully transferred to the sftp server.

There is no long-term archival copy of the data resident at LRL-CAT. Therefore, the User is urged to verify the integrity of the data upon receipt. LRL-CAT cannot accept responsibility for archiving of the User's data.

### 3.6.3. User Account Information

#### 3.6.3.1. With FedEx

The User will provide LRL-CAT with a Federal Express® account number to charge for the return shipment of the sample Dewar.

#### 3.6.3.2. With APS

In the unlikely event that LRL-CAT must purchase miscellaneous materials or supplies as part of your data collection, the User must have an active APS User Account that LRL-CAT personnel are authorized to use.

## 3.7. Additional User Information

### 3.7.1. Loss of Data Collection Capability

If either the APS or the LRL-CAT beamline is not available due to a reason not related to APS equipment, LRL-CAT will endeavor to make up the lost beamtime as soon as possible. In cases where this type of problem occurs near a long maintenance shutdown

of the APS, it may be at least ~1.2 month before LRL-CAT will be able to reattempt the requested data collections.

### 3.7.2. Publication Acknowledgments

All publications that result from work at LRL-CAT must be properly acknowledged in accordance with standard APS Policies.

The following are the required acknowledgments for resources provided by Eli Lilly and Company, the LRL-CAT beamline and the Advanced Photon Source (APS). They MUST be included in all published reports of work undertaken by LRL-CAT (LRL-31ID-D), including journals, books, conference proceedings, or other printed technical media.

#### 3.7.2.1. APS Acknowledgment Statement

This acknowledgment is required under the terms of all APS User Agreements.

"This research used resources of the Advanced Photon Source; a U.S. Department of Energy (DOE) Office of Science User Facility operated for the DOE Office of Science by Argonne National Laboratory under Contract No. DE-AC02-06CH11357."

#### 3.7.2.2. LRL-CAT Acknowledgment Statement

In addition to the APS Acknowledgment, the following should be included in publications that reference data obtained at LRL-CAT.

"Use of the Lilly Research Laboratories Collaborative Access Team (LRL-CAT) beamline at Sector 31 of the Advanced Photon Source was provided by Eli Lilly and Company, which operates the facility."

### 3.7.3. Notification of Publications

All Users will provide a copy of any material submitted for publication that is based on work conducted at LRL-CAT beamline to: us_lrlcat_guinfo@lilly.com. The User is also required to provide similar information to the APS. Further APS publication information can be found HERE.

# 4. Materials and Services

Sources for materials and services described above are as follows:

- For Loops and Pins: Hampton Research
- For Bases:
  - Molecular Dimensions, MD7-401 or MD7-400.
- For UniPucks:
  - MiTeGen, UniPuck Starter Kit: (SKU) M-CP-UPSK001
  - Molecular Dimensions, UniPuck Starter Kit: MD7-600
- For Dewars: Taylor-Wharton (CX100B-11M) Dry Shipper
  - Cole Palmer
  - Cryodepot
  - Fisher Scientific

For Shipping:

Federal Express® http://www.fedex.com/us/

# 5. Contact ID Request Form

Enter the following contact information and email to us_lrlcat_guinfo@lilly.com. A contact identification number will be assigned to you after your information has been submitted. The contact ID will be emailed to the address entered. It is to be used for all sample spreadsheets submitted to LRL-CAT.

**Required fields are indicated by an asterisk (*).**

The contact information provided will only be stored by LRL-CAT for sample identification purposes and dewar return. Filling out this form denotes your consent for LRL-CAT to store this contact information. Please email us_lrlcat_guinfo@lilly.com to request deletion of your contact information from our database.

**Required fields are indicated by an asterisk (*).**

First Name:* _____Last Name:*_____

Position: _____

Organization name:*_____

Organization's web address: _____

Work Phone:* _____

Address 1:* _____

Address 2: _____

Address 3: _____

City:* _____State:* _____ Zip / Postal code:* _____

Prov. / County: _____Country:* _____

E-mail:* _____2nd E-mail: _____

**SFTP account information:** (Leave blank if option to retrieve data from LRL-CAT server is the preferred method).

Server name :*_____

User name :* _____

Password :* _____

Directory path : _____

**FedEx Account Number for Dewar Return: _____**

# 6. Express Crystallography Check List

The following is a Check List of all forms to complete and all materials to procure for successful use of the LRL-CAT Express Crystallography program.

**FORMS TO COMPLETE:**

**LRL-CAT:**

- Complete the Contact Form (Section 5) and email to: US_LRLCAT_GUINFO@LILLY.COM.
- Obtain 1D barcode labels from LRL-CAT at: US_LRLCAT_GUINFO@LILLY.COM.
- Obtain and complete the Sample Spreadsheet (screening and data collection instructions) at: US_LRLCAT_GUINFO@LILLY.COM.
- Return the completed Sample Spreadsheet to: US_LRLCAT_GUSAMPLES@LILLY.COM
- Obtain the complete description of the Express Crystallography service and procedures at: http://lrlcat.lilly.com.
- SAMPLE PREPARATION (Section 3.2) and DOCUMENTATION (Section 3.3).
- DATA TRANSFER**:** Either provide information to connect to a User's tested sftp server or ask beamline staff for an account in our sftp server (See Section 3.2.7).

**Advanced Photon Source (APS) | (For Non-Proprietary Users only)**

- Register with the APS @ Users-Information/Getting-Started/User-Checklist to receive a badge number.
- Complete and submit a "Rapid Access" General User Proposal or request additional beam time at LRL-31-ID-D referencing your GU number at the Submit a Proposal Login.
- Once we confirm receipt of your proposal and approve beam time, submit an (ESAF) at the Complete an Experimental Safety Assessment Form Login.

**MATERIALS & EQUIPMENT NEEDED:**

- Obtain Cryo-Caps : Molecular Dimensions (MD7-400, MD7-401)
- Obtain UniPucks
  - MiTeGen, UniPuck Starter Kit: (SKU) M-CP-UPSK001
  - Molecular Dimension, UniPuck Starter Kit: MD7-600
- Obtain 18 mm Cryo-Loops from: Hampton Research
- Obtain Taylor-Wharton standard dry shipper (TW CX100B-11M) at: Cole Palmer, Cryodepot & Fisher Scientific

# Appendix A

## 1. Legal Terms

"User Data" means all data and information generated by Eli Lilly and Company (Lilly) on User Materials in the performance of the Data Collection Services or provided to Lilly by User or User Institution.

"User Materials" means all biological or chemical materials provided by User or User Institution to Lilly, including User Crystals.

"Data Collection Services" refers to all activities undertaken by the personnel of LRL Collaborative Access Team ("LRL-CAT") with User Materials in order to acquire User Data. These services are described in detail by this website and its associated documents.

## 2. Indemnification

User Institution shall indemnify, defend, and hold harmless Lilly, the directors, officers, and employees of Lilly and the successors and assigns of any of the foregoing (the "Lilly Indemnitee(s)"), from and against all claims, losses, costs, and liabilities (including, without limitation, payment of reasonable attorneys' fees and other expenses of litigation), and shall pay any damages (including settlement amounts) finally awarded, with respect to any claim, suit or proceeding (any of the foregoing, a "Claim") brought by Third Party against an Lilly Indemnitee, arising out of or relating to: (a) the use, handling, transfer or storage of the User Materials or User Data; or (b) a claim that the use by Lilly, User or User Institution of User Materials or User Data, infringes the intellectual property rights of a Third Party; except, in each case, to the extent caused by the gross negligence or willful misconduct of a Lilly Indemnitee and provided further that Lilly provides User Institution with prompt notice of any such claim and the exclusive ability to defend (with the reasonable cooperation of Lilly) or settle any such claim.

## 3. Limitation of Liability

No Lilly Indemnitee will be liable for any Claims incurred by User or User Institution as a result of Lilly's performance of Data Collection Services, unless such Claim is due solely to Lilly's gross negligence or willful misconduct. IN NO EVENT SHALL EITHER Lilly BE LIABLE FOR SPECIAL, CONSEQUENTIAL, INCIDENTAL, OR INDIRECT DAMAGES (INCLUDING WITHOUT LIMITATION LOSS OF PROFIT) WHETHER OR NOT USER INSTITUTION HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH LOSS, HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, ARISING OUT OF THIS AGREEMENT. THESE LIMITATIONS SHALL APPLY NOTWITHSTANDING ANY FAILURE OF ESSENTIAL PURPOSE OF ANY LIMITED REMEDY.

## 4. Warranty; Disclaimer

Lilly will use commercially reasonable efforts in performing Data Collection Services. User Institution acknowledges that the provision of Data Collection Services is subject to availability of the Advanced Photon Source. Lilly specifically disclaims any guarantee that the Data Collection Services will be successful, in whole or in part and that User

Data will be successfully obtained from User Crystals. EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT, Lilly MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, WITH RESPECT TO THE MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE USER DATA, INCLUDING WITHOUT LIMITATION, ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT OF THE INTELLECTUAL PROPERTY OR OTHER RIGHTS OF ANY THIRD PARTY.

**5. Force Majeure**

Lilly shall not be liable to the User or User Institution for damages or losses on account of failure of performance by the defaulting Party if the failure is occasioned by war, strike, acts of terrorism, fire, earthquake, flood, lockout, embargo, governmental acts or orders or restrictions, failure of the Advanced Photon Source or any equipment, failure of suppliers (including, without limitation, energy suppliers), or any other reason where failure to perform is beyond the reasonable control and not caused by the negligence, intentional conduct or misconduct of Lilly and Lilly has exerted all reasonable efforts to avoid or remedy such force majeure; provided, however, that in no event shall Lilly be required to settle any labor dispute or disturbance.

**6. Acceptance of Terms and Conditions**

Submission to the APS of a General User Proposal for LRL-CAT by or on behalf of User shall constitute acceptance of the above terms and conditions by User and User's Institution.