1. Agenda of Working Group 1, held at Warwick, 6th January 2011

1. Chairman's report – Martin Noble
2. Manager's report – Keith Wilson
3. STFC, national and international collaborations – Martyn Winn (Paper circulated in advance)
4. Consultations
    a. Extending support period for KW through 2012
    b. Running CCP4/BCA Summer School 2012
    c. Prioritising data reduction as an area for investment of CCP4 resource
    d. Shape and theme of the next CCP4 grant
5. Executive committee
6. A.O.B.

2. Minutes of Working Group 1, held at Warwick, 6th January 2011

Present:

Martin Noble (Oxford) - Chairman
Keith Wilson (York)
Andrew Leslie (MRC-LMB)
John Helliwell (Manchester)
Dave Brown (Pfizer)
Nicholas Keep (Birkbeck)
Paul Race (Bristol)
Leo Brady (Bristol)
Peter Moody (Leicester)
Ben Bax (GSK)
Ian Tickle (Astex)
Mark Banfield (JIC)
Ralf Flaig (DLS)
Mark Roe (Sussex)
Gwyndaf Evans (DLS)
Frank von Delft (Oxford)
Simon Phillips (RCaH)
Kate Brown (Imperial)
Vilmos Fulop (Warwick)
Pierre Rizkallah (Cardiff)
Jon Grimes (Oxford)
Garib Murshudov (York)
Helen Walden (CRUK)
Phil Evans (MRC-LMB)
Arwen Pearson (Leeds)
Martin Walsh (DLS)
Eugene Krissinel (STFC)
Roberto Steiner (Kings)
Dennis Veselkov (Kings)
Ivan Laponogov (Kings)
Kevin Cowtan (York)
Charles Ballard (STFC)
Martyn Winn (STFC)

Chairman's Report (attached)

Some additional notes, and actions arising:

4.2: Thanks recorded to Martin Noble and Elspeth Garman for their organisation of the 2010 Summer School. Airlie McCoy has offered to organise the next southern meeting in 2012, and the meeting agreed this was a good idea. Gwyndaf Evans confirmed that Diamond would be happy to host the meeting.
Action: Martin to accept Airlie's offer.
Action: Gwyndaf to check Diamond venue e.g. facilities for computer tutorials.

4.3: Nick Keep asked if a re-write of Mosflm could be added to the CCP4 grant renewal. Martin replied that this was a possibility, but the strategy for the grant renewal is currently uncertain, see section 3.4. The meeting discussed whether there were other scientific areas that could compete with data processing. Frank asked about data export after structure solution. This was felt to be a job for the core team, when liberated from more routine duties. Another area is ligand handling. Nevertheless, the meeting felt that better data processing was crucial, and agreed that the area should be prioritised. Dave Brown asked whether the proposed work would include real time data processing? Andrew Leslie felt that would be an extension - the first aim would be to reproduce current functionality using newly written software.

Action: Executive committee to explore how best to contribute to a collaborative development for data processing software. The project is to be initiated as soon as possible, and a full implementation plan to be presented at next year's Study Weekend.

4.4: Historically, the CCP4 grant has included both core support and well-defined scientific projects. In future, we may need to separate these. In particular, funding for core support is hard to obtain, although recognised as vital to the longevity of CCP4.

The current CCP4 grant went into BBSRC's Tools and Resources fund. That fund is primarily for pump priming, and there is a question whether CCP4 can go that route again, and whether the fund

will still exist after BBSRC publishes its detailed plan in early 2011. We need to consider other funding sources, including MRC and Wellcome. There was a suggestion to try an Industrial partnering award, where commercial licences represent the industrial component. The Chairman welcomed any suggestions. We will need to have a plan ready by summer 2012.

Action: Executive committee to consult directly with BBSRC and other stake holders on possible funding routes.
Action: All to send ideas on CCP4 funding to Martin.

4.1: Keith left the meeting for this action. Although the long term aim is for Eugene to take over all duties, it was generally felt that Keith's experience was still vital to the running of CCP4. The meeting agreed to extend Keith's contract. There was a request that his role was well-defined, in particular in relation to the Eugene's role as team leader, and Karen as admin support and possible organiser of meetings.

Action: Martin/Keith to produce job specification.

Keith's report

Keith summarised the financial report produced by Charles. The move of STFC finances to Shared Services has made it more difficult to track income and expenditure. There is a high degree of uncertainty in CCP4's finances, but with the recruitment problems we expect to underspend this F/Y. In the longer term, we appear to have a surplus, but we need to bear in mind possible difficulties over the grant renewal.

It was asked whether CCP4 should make a high level representation to STFC regarding the problems with Shared Services. While this is a legitimate grievance, it is unclear what STFC could do in response - they are forced by central government to use a separate organisation for finances over which they have little control, and CCP4's frustration is felt equally across other sections of STFC.

Bids are in for the tender for Study Weekend 2012. There was the annual discussion on whether January was the best time of year, and the meeting again agreed it was. The matter of industrial sponsorship of the Study Weekend was raised. In general, it is felt that it is better to retain the character of meeting, rather than try to attract a minimal amount of extra revenue.

Action: Core team to get feedback on this SW, and choose site for next year

It is 3 years since the last industrial fee increase. The current price of £9,500 is conveniently just under 10k. We are still cheaper than competitors (although we have a site rather than global licence). The commercial income remains healthy, and we get regular new enquiries.

Action: Revisit commercial licence fee at next year's meeting.

AOB

The science topic of the next Study Weekend will be discussed at the next Working Group 2 meeting on 26th January. Phil Evans reported that the next in the cycle is data processing, and WG1 supported this suggestion.

Martin Walsh gave a presentation on the Diamond Phase III beamlines. Two MX-related proposals are going into the 2nd round of the call, and community support is vital. It was commented that users generally ask for the beam time they think they can get, rather than the beam time that they need, and this gives the appearance that the MX community has enough beam time for its use.

Martyn Winn had circulated an email regarding CCP4's involvement in the INSTRUCT Associate Centre for computational structural biology (CCISB). He informed the meeting that some future CCP4 activities may be done under the auspices of CCISB. This was felt to be a useful way of leveraging additional funding.

Election to the Executive

There is one nomination for a person to replace David Rice on the Exec. In addition, the meeting agreed that the Exec should include an industrial rep. The UK industrial community should nominate this rep. Since their regular meeting is not until November, they will discuss by email.

Action: Dave Brown, Ben Bax, Ian Tickle to consult colleagues and propose industrial representative on Exec.

3. Chairman's report

3.1 Outreach

3.1.1 Study weekend

We would like to thank everyone who contributed to the great success of the 2010 study weekend, "From Crystal to Structure with CCP4" organized by Keith Wilson (York), Kevin Cowtan (York) and Paul Emsley (Oxford).

This year's meeting, organized by Roberto Steiner (King's College, London) and Bernhard Rupp (k. k. Hofkristallamt (USA)) is titled "Model Building & Refinement & Validation", and maintains this meeting's tradition of assembling an excellent list of speakers.

3.1.2 BCA/CCP4 Summer School on Computational Crystallography

This year's Summer School was organized by Elspeth Garman and Martin Noble and took place in Oxford, 5th-9th September. In a highly over-subscribed course (approximately two applicants per place), 45 students from across the UK and EU were able to study many aspects of macromolecular crystallography in depth. The organizers were extremely grateful to the local and invited speakers, and especially to Airlie McCoy (CIMR, Cambridge), Peter Artymiuk (Sheffield), Nick Keep (Birkbeck), and Ed Lowe (Oxford), whose collective contributions ensured another outstanding level of satisfaction in the end-of-course anonymous feedback.

3.2 Scientific highlights (no particular order)

The core of the suite continues to evolve under the careful supervision of **Eugene Krissinel, Charles Ballard** and **Ronan Keegan**: version 6.2 is approaching readiness, with 6.1.24 being effectively a beta for the new release. New effort is being put into streamlining the infrastructure for maintenance and distribution. Improving these has been identified as a way in which we can enhance both user and developer experience, and therefore devote more resources to the development of new algorithms and automated implementations: this in turn is ever more important as the Phenix Consortium and Global Phasing continue to improve their offerings.

Our headline scientific ambition for the current grant has been to improve the handling of low resolution and otherwise challenging data. This year we can feel that we are ahead or at the forefront in these areas. Enhancements in REFMAC make it the best program in the world for refining structures against twinned data, while the implementation of "jelly restraints" (a form of local NCS) are transformative in the effectiveness of REFMAC in refining moderate resolution structures, especially where a high resolution template can be used as an external restraint. At the same time, BUCCANEER continues to forge ahead as an excellent tool for automatic interpretation of medium and low-resolution structures. This year has seen progress with the outstanding challenges of model completion and loop building, the latter of which should be complete in the next year.

Incorporating exotic chemical species into structures continues to be more difficult than we would like. We are formulating a comprehensive strategy as to how CCP4 can help to make the community's collective head ache about this go away: immediately, work in JLigand (implemented in **Garib Murshudov**'s group and integrated into the package by **Natalie Zhao**) , ProDRG (developed for CCP4 by **Alex Schuettelkopf** in the group of **Daan van Aalten**) and Coot (propelled ever onwards by **Paul Emsley** and the group of **Kevin Cowtan**) is providing accessible tools for building and appropriately restraining chemical structures.

MOSFLM remains the suite's robust work-horse for extracting intensity estimates from diffraction data. Work by **Owen Johnson**, **Harry Powell** and **Andrew Leslie** have enhanced the program's stability, functionality, and useability. As we look to the future of data processing (see below), MOSFLM will continue to be a source of know-how and experience for both algorithm and UI.

3.3 Major projects

3.3.1 QtMG

Thanks to the efforts of **Stuart McNicholas,** versions of QtMG from 2.4.3 have seen dramatic improvements in terms of

- Stability: major bugs in symmetry, movie-making, and memory management have been corrected.
- Functionality: the sequence viewer provides a convenient tool to help with the analysis and comparison of structures with different sequences.
- Useability: the implementation of a single-window view, exploiting excellent GUI tools within Qt, is removing the palette overload that earlier versions shared with the majority of molecular graphics packages
- Visual appeal: borrowing from the world of computer games, the use of GLSL shaders has already permitted real time rendering at near-ray-traced quality, and promises to allow for the real time implementation of shadows.

As a result of these developments, it is my view that QtMG has come of age: it has certainly won a place as my own program of choice, in preference to software that I have written myself.

3.3.2 GUI/Automation

In the period since the last WG1 meeting, our effort has been devoted towards identifying the appropriate technical solution to meeting the automation needs of CCP4 users. This has involved an extensive consultation and trialling process among developers with representatives from industry, and been coordinated in two dedicated meetings of developers. Special thanks are due to **Fei Long**, **Liz Potterton** and the core team for their significant work in evaluating our options. Our strategy can be summarised as follows:

- CCP4 functionality and data-types will be encapsulated in python classes that provide a light-weight mechanism to assemble workflows with complicated logic
- Substantial functionality assembled from these elements will be further wrapped as EDNA classes to allow their use/reuse in the heavier-weight pipelining framework employed at DLS
- Pipeline and project history will be captured in a database so as to facilitate inter-step communication of program and project metadata, history interrogation, and report-generation.
- A graphical front end to the history and control of workflows is being prepared using tools from the webkit-integrated Qt suite. GUI development will be pursued in a highly modular way, in anticipation of an evolving landscape for crystallographic computation which may involve more use of web-based and GRID resources.

Liz Potterton has taken scientific lead in the GUI development, with **Eugene Krissinel** coordinating the overall automation strategy, and **George Pelios**, working under **Charles Ballard**, to initiate database code development.

3.3.3 Relocation

In line with the wishes of WG1, the core team has now moved to the Research Complex at Harwell (RCaH), where **Eugene Krissinel** has taken up the leadership role. The community will know Eugene well from his work: SSM identifies distant similarities between your protein and others in the PDB and also superimposes models based on automatically identified secondary structural

equivalences within Coot and QtMG; PISA identifies and analyses putative biological oligomers apparent in crystallographic structures; the MMDB coordinate manipulation libraries underpins Coot, QtMG, and indeed much of the CCP4 suite. Eugene's experience in the generation of high performance, industrial strength computing algorithms will be invaluable in taking the suite to the next level. As well as coordinating CCP4 software development, Eugene will continue to contribute novel code and algorithms: he has already begun development of the next-generation of SSM (called ESFC), and CCP4srs, a template for how to achieve unified ligand functionality across CCP4.

Within the RCaH, Eugene is joined by the established core programmers **Ronan Keegan** and **Charles Ballard**. Ronan's experience with the development of MrBUMP makes him the ideal person to implement crystallographic pipelines. The DIMPLE pipeline, an automation of structure determination tuned to the ligand-soak/co-crystallisation use-case, has been developed in close collaboration with colleagues at the Diamond Light Source. This pipeline, which is being deployed on all of the DLS beamlines, is the first concrete product of the synergy between CCP4 and DLS. Charles continues to play a crucial role in the development, distribution, and maintenance of the suite, as well as in navigating the complexities of CCP4's financial and organisational status within the STFC.

Recruitment and retention within RCaH has been an area where we have encountered setbacks and where the climate is troubling. Our two appointments to Core Team positions have not lasted: in one case our appointee's family circumstances made a resignation unavoidable, and in the other a decision was taken not to employ beyond probation. The financial climate has restricted our freedom to refill and indeed expand the core team so as to recapture critical mass in the new location. We have lodged an appeal in the face of the STFC's hiring freeze, and we aim to prosecute this to the fullest in order to support our staff.

3.3.4 Distribution

In light of the difficulties in maintaining staff numbers in the Core Team, it has not been possible to make the sort of revolutionary improvement that we have been looking for in the mechanism of maintaining, distributing, and updating the suite.

3.3.5 PiMS

In line with the decision taken at last year's study weekend, we have extended the lifetime of CCP4's investment in PiMS. This year, a further review was held at which the progress of the project against the deliverables outlined in the last report were assessed. **Chris Morris** has strengthened the package this year, improving performance, the UI consistency and browser neutrality. While the technical developments are, as ever, excellent, there remains something of a gulf to cross in terms of take-up. Although the system remains invaluable to high-throughput sites, the uptake in small and medium size laboratories, and especially in industry, is still underwhelming. In light of this, the project plan agreed last year was subject to some refinement. Specifically, to ensure that the investment to date benefits the broadest possible community, it was decided to focus on developing PiMS as enabling technology for sites to which the community as a whole has access, and from which we are all able to derive benefit. In particular, a proposal was made to promote PiMS as the back-end infrrastructure in OPPF and at each of the INSTRUCT associate centres. For direct application in small and medium laboratories, it was decided to focus resources on xtalPiMS, both as a standard tool for monitoring crystal growth, and as a streamlined vehicle through which to transfer sample information to synchrotrons.

4. Consultations

4.1 Extending support for KW through 2012

CCP4 currently provides 20% salary support for KW reflecting his time spent in management of the core team and representation of CCP4 interests at the national and international level. Over time, it is intended that this activity will be devolved to the CCP4 Team Leader in the RCaH, and to the Chairman and members of the executive committee. With WG1 approval, I would like to defer the end date of that transition to reflect current challenges in terms of a) The pressure on the core team due to recruitment and retention, which requires the Team Leader to be directing his time to development and Core Team activities, and b) the difficult funding environment which means that CCP4 needs to be connected with more different funding streams to ensure long term sustainability.

4.2 Future organization of Southern UK Summer School

After hosting the South of UK Summer School in 2006, 2008, and 2010, EFG and MEMN feel it appropriate to allow another organizer to have a turn. Airlie McCoy, who has shouldered the lion's share of the teaching in recent years, and who consistently rates as one of the most highly appreciated course tutors, has kindly offered to take up the challenge. With WG1 permission, we would like to invite her to press on with the arrangements to run the course: these will need to be begun all too soon.

4.3 Prioritising data reduction as an area for investment of CCP4 resources

For the past 25 years, Mosflm has provided invaluable service as a program for extracting intensity estimates from raw images. On-going algorithmic developments by Harry Powell and Andrew Leslie have kept it competitive with other packages in this area, while the introduction of the modern iMosflm GUI has made it accessible and informative: this has made it an excellent tool for teaching and learning as well as for routine data reduction.

Despite its many strengths, the venerable code-base on which MOSFLM is based makes it hard to maintain in the long term, and presents a barrier to MOSFLM's use and integration into software pipelines by third parties. It may also present challenges to the development of new approaches to data analysis suited to ultra-fine phi slicing, open aperture data collection, new detector geometries, and other experimental developments.

For these reasons, CCP4 proposes to invest resources into a partnership to develop the next generation of openly accessible data reduction software. Discussions have been initiated through Andrew Leslie with representatives of the Diamond Light Source, and additional possible funding streams are being explored to support this ambitious project. We would like to seek WG1 approval for making this a funding priority area for CCP4, just as molecular graphics has been in recent years, giving rise to our support for the COOT and QtMG programs.

4.4 Shape and theme of the next CCP4 grant

The current BBSRC/MRC grant, which sustains 3+1 scientific and one administrative post, will expire in September 2013. Over the course of this year, the executive committee will be formulating grant proposal(s) to support this activity beyond the current grant. Input from WG1 on the strategy and/or scientific theme for such applications would be welcome at this meeting, or through the course of 2011.

5. Executive committee

The current constitution of the executive committee is as follows:

Martin Noble	**Chair CCP4, elected 2010, begun 2011**
David Rice	**Elected. Jan 2008. Leaves end of 2010.**
Peter Moody	**Elected. Jan 2009**
Frank von Delft	**Elected. Jan 2010**
Phil Evans	**Ex officio: elected Chair WG2**
Keith Wilson	**Ex officio: Scientific Coordinator CCP4**
Eleanor Dodson	**Co-opted**
Garib Murshudov	**Co-opted Jan 2007. Previous Member.**
Kevin Cowtan	**Co-opted**
Randy Read	**Co-opted**
Martyn Winn	**Co-opted: STFC representative**

We note that David Rice's elected term comes to a close at this Study Weekend, and would like to thank him for his involvement. Accordingly, there is now a place available for an elected member, and we would like to invite nominations. Executive committee has been slightly underused this year (a further victim of the hiatus associated with recruitment and retention), but at its best it can be a body that helps make key strategic and scientific decisions that impact the suite significantly. We would welcome new blood, from people with ideas, energy, and time to get closely involved in the oversight of the package. Naturally, we would hope that people nominated had been canvassed as to their willingness to serve if elected in advance of their nomination. Nominations will be accepted at the meeting, or may be e-mailed in advance to me (martin.noble@bioch.ox.ac.uk)

I apologise for the extremely short notice on this: if we have received less than two nominations by the time of the WG1 meeting, we will defer the election to the end of this month, with voting to take place by e-mail.

We further propose to establish a position on the executive committee to be held by a representative drawn from our commercial users. This proposal is open to discussion at this meeting.

6. MDW Report on INSTRUCT Associate Centre

As many of you will know, INSTRUCT is a major initiative to build up a European infrastructure for structural biology (http://www.instruct-fp7.eu/). It consists of a number of centres/facilities linked by a common management framework. In 2009, the INSTRUCT management issued a call for an Associate Centre in Computational Structural Biology. A UK consortium, including representatives of CCP4, CCPN, DLS and others, bid for this and was successful. The Associate Centre ("CCISB") is formally based at the Research Complex around the CCP4 core group, although it incorporates others groups around the UK.

While INSTRUCT has been in the Preparatory Phase, CCISB has not been very active. However, the Implementation Phase of INSTRUCT starts on April 1st 2011, so things will start to happen. How does CCISB relate to CCP4? If INSTRUCT is successful, then CCISB could be a major activity involving CCP4. Nevertheless, we are conscious that there must be no negative impact on CCP4 interests (or funding), and will proceed cautiously. We hope that CCISB will help to provide an exciting scientific environment for CCP4, and give opportunities for future collaborative projects.

CCISB is a partner on two recently-submitted EU proposals (eSB-Environment and BiomedBridges) which, if successful, would yield additional posts at the Research Complex working closely with the CCP4 group. There have also been some initial moves towards the formation of a CCP for electron microscopy. The current plan is that the CCP would be coordinated from the Research Complex, as part of CCISB, in order to benefit (amongst other things) from co-location with CCP4.