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Index:

1. About Instruct: Introduction

One of the grand challenges in biology is to combine structural biology with cell biology so that an atomic level dissection of the cell can be reconstituted into a functional system, including its temporal dimension. Instruct has now brought together the key technologies into a single infrastructure to enable scientific discoveries that promise momentous impact in the life sciences by providing peer-reviewed access and training to empower the User community. Instruct accelerated into operations via a transition stage that started with a simple legal framework in 2011 and will now move to the long-term stability of ERIC status.

Huge technological developments in structural and biochemical methods now allow structural biology to provide detailed mechanistic information about biological macromolecules and complexes that underpins our understanding of biological processes in healthy and diseased cells. Its vast impact on biomedical research as evidenced by recent Nobel prizes awarded for the structure of the ribosome (2009, the major antibiotic target), the structure of GPCRs (2012, proteins targeted by ~40% of all current drugs) and dynamics methods (2013). Achieving such breakthroughs requires access to cutting edge instruments and techniques for the analysis of biological structures at different resolution ranges, from atomic to cellular, and combining these results in an integrative approach. Instruct is the vehicle delivering integrated approaches to structural biology. Generally these services are not commercially available and currently no other infrastructure in the world that provides the multi-platform, integrated format available to Instruct Users. Thus Instruct will promote innovation and discovery in biomedical science, helping to define a strategic plan for structural biology in Europe to develop the European Research Area, supporting the biotechnology and pharmaceutical industries meeting the Grand Challenges of Horizon 2020.

Instruct aims to specifically support research that uses integrated approaches and technologies. Since 2011 it has provided increasing **peer-reviewed access for Users** to a broad integrated palette of state-of-the-art structural biology equipment and know-how; facilities include all major technology subcategories. Instruct supports access with **expert staff on-site** and **training for Users** of the instrumentation. A particular strength of Instruct lies in the selection of Instruct Centres that are recognized for their outstanding technical expertise and international recognition in specific areas of biological research. Open access to this additional know-how through an international infrastructure is unique.
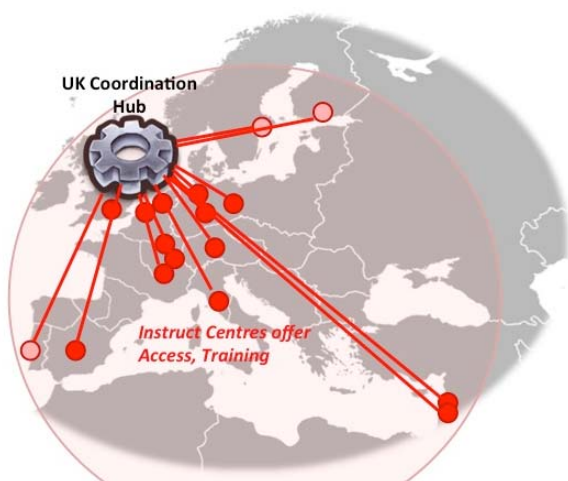
Instruct Hub-Node model. Instruct offers, through the Instruct Access Management System at the Hub, a **single point of access** to multiple techniques at one or more distributed Centres of exceptional quality, which have developed unique expertise offered as **Flagship platforms**. Instruct provides a coordinated route to access the key technologies needed for the best scientific outcome: *i.e.* open access with expert support and supervision with advice on other methods, technologies or approaches that might be useful both for expert and non-expert Users (including those in clinical research). This strategy allows scarce, highly expensive instrumentation combined with the necessary expertise and training capacity, to be made available for international access and promotes dissemination of technical advances.

This document describes the objectives of Instruct and provides a snapshot of its operations from the Transitional Phase of operations (2011-2015). Sections 1-4 demonstrate the current operational

model of Instruct by which Instruct already meets the five specific requirements of Article 4 of the ERIC Regulation. Current policies that can be directly transferred to Instruct-ERIC or further implemented when needed, are noted and where appropriate provided in Annexes. Section 5 describes the case for the Instruct-ERIC and subsequent sections describe the Instruct-ERIC.

2. Principal objectives of Instruct: Access and Training

Access*: Instruct services the above mission through its distributed Centres via peer-reviewed open access for Users to a broad palette of state-of-the-art infrastructure.*

Instruct provides open access to technologies at institutional, regional or national facilities, representing the most advanced or specialist in the field of structural biology. Users are guided by experts to optimize the research outcome whilst providing practical training. Access is through the online proposal submission portal: https://www.structuralbiology.eu/update/submit-proposal and follows the process outlined in the diagram.

The Instruct Access Policy and Procedures (Annex 1: will apply also to Instruct-ERIC) defines the principles of access provision and the procedures for delivery of access at Instruct Centres. Access rules for provision, eligibility and funding are available at: https://www.structuralbiology.eu/resources/proposal-submission/who-qualifies. Guidelines for applicants, Moderators and Reviewers are available online at https://www.structuralbiology.eu/resources/proposal-submission/guidelines-moderators-and-reviewers .

The overarching criterion for approval is scientific excellence. Once granted, access is managed locally by a Centre (by the Centre Coordinator) in coordination with the Instruct Hub and progress is monitored using the online tools of the proposal system. The Centres and the Hub ensure that Users are closely chaperoned through an access workplan. Outcomes from the programme to date demonstrate success (more than 100 peer-reviewed publications acknowledging Instruct as a result of access to Instruct infrastructure). Instruct funded access to the infrastructure requires the agreement to publish data, duly acknowledged, arising from the work undertaken at a Centre. For Users undertaking proprietary work, access is through a fee for service agreement which is negotiated separately with the Instruct Centre. The Access Funding Policy, which will apply to Instruct-ERIC is summarised in Section 7 of this document.

Training*: Europe will require at least one million more researchers in the next decade to reach the target of investing 3% of EU GDP in R&D by 2020[1]. Instruct training programmes contribute by increasing the skills level of researchers in structural biology.*

Instruct provides training in for the new User, and more specialist training for those wishing to expand their skills. It also provides a community of technologists and researchers who can increase standards and support students to develop their careers in science.

Instruct opens calls on a regular basis for training courses, workshops and symposia in technologies and methods for integrated structural biology research, including data management. Events are

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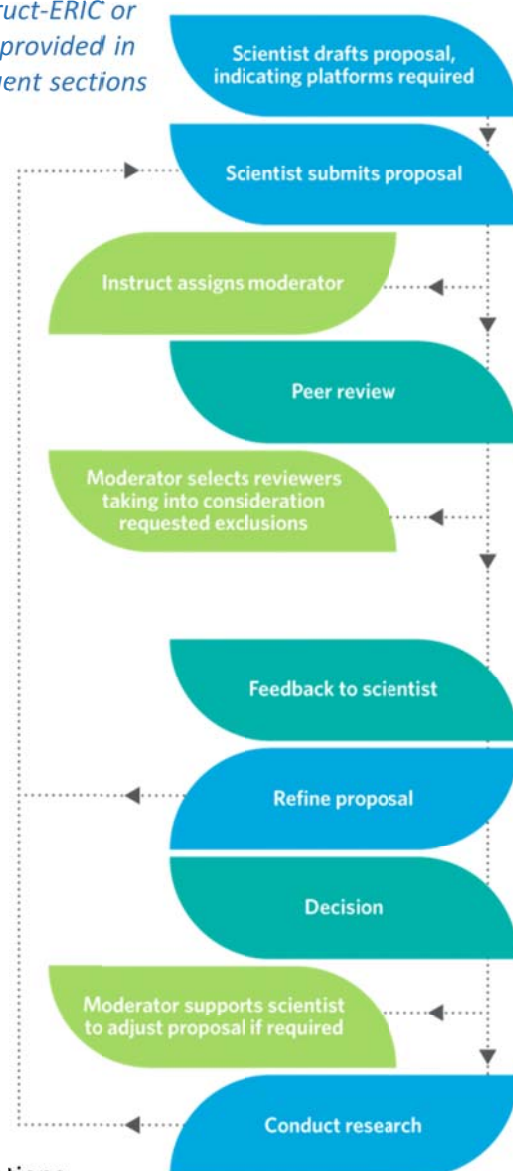
[1] http://ec.europa.eu/research/innovation-union/index_en.cfm?pg=key

generally hosted at Instruct Centres, but may be shared with other RIs or research organisations as appropriate. Courses encourage participants to work on their own research problems, including undertaking wet-lab experimental processes. The training programme (*https://www.structuralbiology.eu/support/whats-on/calendar-events)* has operated successfully since 2012 and is in high demand within the Instruct community . This scheme will be maintained by Instruct-ERIC.

3. Instruct Centres and the Instruct Hub

Instruct activities have been delivered during the transition phase at the 16 Instruct Centres distributed across the national Members, mostly embedded in higher education institutions. The Centres provide the organizational framework to deliver Instruct activities to researchers and other stakeholders (technology developers, translational research industries, other research infrastructures, *etc.*). All Centres have at least one Flagship technology in which they specialize but most also offer open access to a varied range of high quality infrastructure and expertise including major structural biology technologies (https://www.structuralbiology.eu/update/platform-catalogue). Presently the Centres comprise:

Instruct Centre-BE (Nanobodies4Instruct), Instruct Centre-Germany1 (Electron Microscopy MPIB Martinsried), Instruct Centre-Germany2 (NMR at CCMP and cell-free expression at Goethe University, Frankfurt), Instruct Centre-Spain (Image Processing CNB, Madrid), Instruct Centre-FR1 (Electron Microscopy, Strasbourg), Instruct Centre-FR2 (NMR IBS, Grenoble), Instruct Centre-IL (protein purification ISPC, Rehovot), Instruct Centre-IT (NMR CERM/CIRMMP, Florence), Instruct Centre-NL (Electron microscopy NeCEN, Leiden; protein facilities NKI, Amsterdam; NMR Bijvoet Center, Utrecht); Instruct Centre-UK (Mammalian protein expression STRUBI, Oxford; Electron microscopy OPIC, Oxford; baculovirus expression OPPF, Harwell; X-ray technologies Diamond Light Source, Harwell), Stable Protein expression Centre Braunschweig, Virus purification Centre Helsinki, Bioinformatics Centre Tel Aviv, solid state NMR Centre Berlin, Mass Spectrometry Centre Utrecht and Oxford, Computational Biology Centre Harwell.

Centres typically offer the latest high specification instrumentation and aim to make these accessible to Users with limited background in structural methods by providing training and support for experimental design, data collection and data analysis. Centres may also offer access to more specialist expertise, where new methods and approaches are made available to Users, pushing the boundaries of technology and bringing it to a broad user base.

The Instruct Centres are at the heart of Instruct activities and form the Core of the infrastructure to:

- Provide technology/expertise of world-leading standard;
- Provide facilities and expertise that fit with Instruct strategy;
- Provide the expertise necessary to support Users and technical development (as appropriate);
- Promote and participate in collaboration (European/international) that drives technical development;
- Demonstrate the power of integrative technological approaches to structural biology research.

These are codified into the criteria for the selection of Instruct Centres (these criteria will apply to Instruct-ERIC and are reported in Annex 3 of the Instruct-ERIC Statutes). Centres have been and will continue under Instruct-ERIC to be selected and reviewed by the Instruct Council who will take recommendations from the Independent Scientific Advisory Board (this will apply to Instruct-ERIC, see Articles 13.7 and 15 of the Statutes).

Technologies available at Instruct Centres: **The Instruct infrastructure includes electron microscopy, NMR, X-ray methods, protein production, mass spectrometry and other biophysical methods to span structural biology, they can be viewed in a catalogue of access platforms on the Instruct website (www.structuralbiology.eu) and access requested via the proposal system.** Each Centre defines an allocation (in day units) of access for Instruct use. Centres provide a cost

calculation per unit of provision of access on the basis of auditable criteria, which enables a component calculation of the in-kind contribution made to Instruct by the Member State. Going forward, Instruct-ERIC will explore ways of engaging with other technologies and major infrastructures as appropriate, for example for the provision of access to neutron scattering.

Instruct Centres play an advocacy role to promote Instruct to existing and potential stakeholders and establish outreach to communities with which they have established connections. The Centres play a key role in disseminating Instruct-related research results to encourage and promote uptake of Instruct infrastructure use. To help in this, **Instruct** facilitates national communities of structural biologists in Instruct Member countries, by providing active on-line networking *fora* via the Instruct website where interest themes or national groups can share experiences. Centres establish and develop relationships with industry, either in translational research, technology development, manufacture and implementation, maintaining Instruct at the methodological forefront.

Selected key technology development with Instruct Centres: proof of principle

In the Transition Phase, Instruct Centres contributed significantly to technology development and implementation. Some examples include:

1. ***Protein Expression***: Instruct Centre- Braunschweig. "Multi-host expression system for recombinant production of challenging proteins." Meyer S, Lorenz C, Baser B, Wördehoff M, Jäger V, van den Heuvel J. PLoS One. 2013 Jul 17;8(7):e68674. doi: 10.1371/journal.pone.0068674.

2. ***Automated protein expression in mammalian cells***: Instruct Centre-Oxford. " Automation of large scale transient protein expression in mammalian cells." Zhao Y, Bishop B, Clay JE, Lu W, Jones M, Daenke S, Siebold C, Stuart DI, Jones EY, Aricescu AR. J. Struct Biol. 2011 May; 175(2): 209-215. Doi: 10.1016/j.jsb.2011.04.017. Epub 2011 May 6.

3. ***Protein Crystallization***: Instruct Centre-Frankfurt. "Automated high-throughput crystallization suited for membrane proteins and more." Thielmann Y, Koepke J, Michel H. J Struct Funct Genomics. 2012 Jun;13(2):63-9. doi: 10.1007/s10969-011-9118-y. Epub 2011 Nov 19.

4. ***Virus purification***: Instruct Centre for Virus Production-Helsinki. "Monolithic ion exchange chromatographic methods for virus purification." Oksanen HM, Domanska A, Bamford DH. Virology. 2012 Dec 20; 434(2):271-7. doi: 10.1016/j.virol.2012.09.019. Epub 2012 Oct 22.

5. ***Electron microscopy***: Instruct Centre-Martinsreid. "Cryo-focused-ion-beam applications in structural biology." Rigort A, Plitzko JM. Arch Biochem Biophys. 2015 Feb; pii: S0003-9861(15)00071-5. Doi: 10.1016/j.abb.2015.02.009.

6. ***Software development***: Instruct Centre-Madrid. "Xmipp 3.0: An improved software suite for image processing in electron microscopy." De la Rosa-Trevin JM, Oton J, Marabini R, Zaldivar A, Vargas J, Carazo JM, Sorzano CO. J. Struct. Biol. 2013 Sep 26. Doi:pii: S1047-8477(13)00256-6. 10.1016/j.jsb.2013.09.015.

7. ***In-cell NMR:*** Instruct Centre-Florence. "[Atomic-resolution monitoring of protein maturation in live human cells by NMR](#)". Banci L, Barbieri L, Bertini I, Luchinat E, Secci E, Zhao Y, Aricescu AR. **Nat Chem Biol**. 2013 May;9(5):297-9. doi: 10.1038/nchembio.1202.

Instruct Hub: Coordination of Instruct activities is undertaken by the Hub, located in the host country (UK). Scheduled regular teleconferences between Instruct Centres and the Hub and communication and management through the various Instruct governmental bodies underpins the delivery of access as the principal Instruct activity and monitors the impact of training and networking activities. The Hub delivers administrative services and reports on impact and added value, using quantitative and qualitative measures. The Instruct Hub and the Instruct Director are currently located at the Instruct Centre, Oxford.

4. Instruct infrastructure fulfils the following ERIC requirements:

a) Necessary for European Research: Europe's position at the forefront of scientific discoveries and pioneering innovation in research is founded on the availability, for its researchers, of internationally competitive scientific infrastructure. Scientific infrastructure opportunities and needs change rapidly

but at a national level it may take many years to respond to these and require considerable investment which may also depend on political will.

Instruct strategy has been to select as its nodes complimentary Centres of excellence where advanced structural biology instrumentation and methods are available in an expert academic setting. Instruct is modular to allow the addition of new technologies as they become available and to benchmark new methods in a number of systems. Instruct strategy is to grow its infrastructure according to need, recognising technological redundancy and re-prioritising the components as necessary. Growth in the infrastructure technologies will be mirrored by expansion of Membership, within the ERA and outside. Expansion and internationalization will strengthen Instruct by providing access to high quality infrastructure for structural biology to the very large and growing international User community (as of 1st October 2015 there are over 3,300 registered users of Instruct). From the User perspective value is added through new opportunities for exploiting synergistic integrative approaches through collaboration, mobility to excellent facilities within the ERA, expert training and increased skills in the latest and developing technologies. All these factors enhance the scientific outcomes of the User's research.

b) Strengthens and helps structure the ERA: Instruct has the capacity to lead to marketable technological developments with companies manufacturing structural biology equipment, and stimulate the development of SMEs. European equipment manufacturers are among the foremost in the world (for example Agilent, Bruker, Gatan, Leica, Qiagen) and Instruct offers them an opportunity to work with the best researchers in Europe to develop and test the next generation of equipment (*e.g.* Instruct has established an MOU with FEI to integrate new instrumentation with software). Thus Instruct will promote innovation and discovery in biomedical science, coordinating with biotechnology and pharmaceutical industries to introduce and adapt technology advances to translational research. Instruct is well positioned to design a combined top-down and bottom-up strategy for future investments in structural biology in Europe. The experience accumulated ideally positions Instruct for describing the future European Infrastructure landscape in structural biology, given the current scientific trends, and with our detailed knowledge of the present situation. Instruct is initiating these actions to deliver such a strategic view, with added perspective from the Instruct Independent Scientific Advisory Board.

c) Provides effective access for European researchers: Instruct was set up to support the structural characterization of biological macromolecules and cellular complexes that are important for understanding fundamental cellular processes that in turn might lead to vaccine or therapeutic target identification. This focused structural proteomics model established in Europe has been widely adopted globally. Instruct specifically supports research that uses integrated approaches and technologies. Integrated access is provided through the purpose-built advanced on-line Access Management System, which not only handles the moderation and peer review of applications for access but also supports users through the process of what may be a complex process of using a series of platforms and also provides audit information, reports and metrics to Instruct management. At present the system is managing over 200 applications and is currently being rolled out to other infrastructures.

d) Enables knowledge mobility and increases the intellectual potential throughout Europe: Instruct's popular training courses and workshops (28 completed as of 1st October 2015) target researchers from the structural biology community at several levels: students (mainly doctoral); postdoctoral researchers; facility technicians; experienced structural biologists exploring new approaches for their research; industrial researchers. Programmes are structured around the needs of these communities and provide the opportunity for hands-on experience and where possible, the ability to work with their own materials to kick-start or expand an existing research project. Courses aim to introduce a degree of standardisation in methodologies, and promote an integrative approach in the structural biology field. Instruct is actively engaged in developing strong links with non-EU countries where structural biology is less well developed than in Europe (e.g. Africa, Americas, Jordan) or where

structural biology is very advanced and developing quickly (e.g. China). Further skills training is offered through the Internship programme and the R&D award programme (see https://www.structuralbiology.eu/content/rd-pilot-project-awards).

e) Contributes to dissemination/optimisation of the RTD results: Instruct activities produce visible results such as high impact publications, conference presentations, and published protocols. Instruct requires structural data to be deposited in public databases where possible and the intended publication of data arising from the approved work is a condition of Instruct funded support for access. In addition to conventional scientific dissemination routes, Instruct constantly updates information via the Instruct website, related and interlinked web portals, newsletters aiming at the wider scientific community and the public, conferences and other events aimed at both scientists and the general public. Instruct is active in the social media through Twitter and Facebook, bringing key messages to a very large audience and enabling an instant engagement and response.

f) Outreach to non-European researchers: The Instruct model allows new technologies being developed outside Europe to be added, to raise standards and increase the portfolio of platforms available for access. Additionally, international cooperation will help in the long term strategic planning of very large-scale facilities and the economies of scale in developing infrastructure in a coordinated and integrated way. The use of remote access to certain facilities will increase, removing boundaries for Users of many technologies (especially X-ray and electron microscopy) and expanding the opportunities for global research. Discussions to establish formal international links are underway (as of 1st October 2015) with China, India, Jordan, South Africa and several countries in South America.

5. Necessity of transition to ERIC status:

Instruct's starting legal form used an International Consortium Agreement setting out the principles of membership, with the Instruct Hub operated by a small not-for-profit limited company. This strategic decision enabled Instruct to enter into operations quickly at limited scale. This was successful, and established the operational, administrative and reporting processes for Instruct, which now provides infrastructure access, training and networking to a large European user base. The success of Instruct has also made clear that it is now urgent to transition to ERIC status. ERIC status is specifically set up to be the optimum legal structure for European Scientific Infrastructures, including distributed Infrastructures such as Instruct. It is now appropriate and timely to transition to Instruct-ERIC for the following specific reasons.

Firstly, certain countries have committed to Instruct on the condition that the Instruct-ERIC is established as this allows a proper positioning on their road-map and facilitates planning for investment in scientific infrastructure.

ERIC status facilitates a proper engagement and ensures that there is direct engagement with the appropriate Ministry and formal national recognition.

ERIC status ensures the long term commitment of the member countries and allows sound financial planning and the opportunity to increase the activity of Instruct, and improve delivery of services to the scientific community.

ERIC status will allow tighter and more effective integration among the Instruct Centres with support for those Centres as well as the Hub at the government level.

ERIC status will allow formal engagement with countries outside of Europe, and with Industry.

Instruct stability will ensure continuity of support for major infrastructure for European scientists working in the field of structural biology, which can otherwise be fragmentary and unstable.
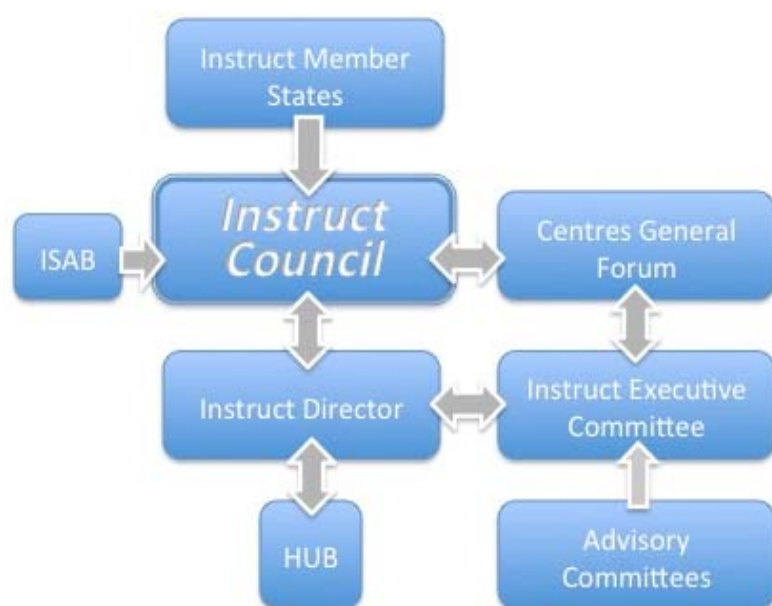
The higher profile of the ERIC will be internationally recognised and will facilitate diverse engagement on the international and commercial stage, for instance to expedite the development of new technologies.

The enhancement will allow employment opportunities to be created by the RI at various levels.

6. Instruct-ERIC Governance and Organisation

Instruct-ERIC will be established as an organisation to coordinate the activities of the Instruct infrastructure. The Governance bodies of the Instruct-ERIC, serving the Instruct Member States will be: Instruct Council, Independent Scientific Advisory Board (ISAB), Instruct Director, Executive Committee and Advisory Committees, Centres General Forum. The governing bodies will be supported by the Instruct Hub (the central management and coordination office) that will work with the Director to ensure the day-to-day management of Instruct-ERIC.

Instruct Council:
- Council will be the primary governing body of Instruct-ERIC and will be composed of representatives of the Members and Observers of Instruct-ERIC. Each Member will have one vote; Observers will have no vote.

- Council responsibilities are defined in Article 13 of the Statutes.

- Council will elect its own Chairperson from among the voting Member representatives by 2/3 majority. The Instruct Director may be invited to attend Council meetings without voting rights.

- The Council Chairperson will delegate to the Instruct Director the operational tasks of Instruct-ERIC to deliver the strategic objectives of the infrastructure.

The *Instruct Hub* and the *Instruct Director* will be located within the Instruct UK Centre, Oxford. The Instruct Director will bear the day-to-day responsibility for overseeing the activities of Instruct-ERIC and leadership for Instruct as a whole as described in Article 14 of the Statutes. The Instruct Hub shall likely include the following other staff members: a Coordinator who will be appointed to take operational responsibility for the day-to delivery of access and other Instruct activities to stakeholders; a Project Manager who will be appointed to deal with EC-funded projects, grant application preparation and follow-up; a Finance Officer and an IT Officer. Recruitment follows the Instruct-ERIC statutes with the Director and senior Instruct staff posts to be appointed, following an open competitive process, by the Instruct Council. Administrative posts in the Hub will be appointed according to a fully transparent recruitment process by the Director.

Independent Scientific Advisory Board (ISAB):
The ISAB shall comprise from five up to eight scientific and technical experts from outside Europe to advise the Director and the Instruct Council on any scientific and strategic matters relevant to Instruct-ERIC (see Article 17 of the statutes). This will include the regular review of results from the Instruct Centres in order to advise on future goals, needs and opportunities for the infrastructure.

Committees:
The *Executive Committee* will be the principal executive management committee for Instruct-ERIC, described in Article 16 of the statutes. The Executive Committee shall comprise representatives (following a call for nominations by the Instruct Council) drawn from Instruct Centres and be tasked by the Director with all general matters related to Instruct activities including drawing up proposals, establishing and modifying workplans and ensuring consistency, coherence and stability of infrastructure services. The Executive Committee will be chaired by the Director.

The Executive Committee will be of limited size, for efficiency, and therefore a *Centres General Forum* will meet at least once per year to ensure representation of the full set of centres, and will also include elected user representation. The report of the Forum will be reviewed by Council.

The Instruct Council may establish a number of advisory committees, for example these might include:
Access Committee – to monitor and manage the delivery of access and report to the Executive Committee with recommendations for operational amendments.
Training Committee – to manage the launch of Training calls, selection, funding and delivery of courses. The Training Committee shall report to the Executive Committee.
Industry Committee - tasked with identifying new industry stakeholders and making recommendations for engagement and the provision of infrastructure aligned with commercial needs and processes. The Industry Committee shall report to the Executive Committee.
IP and Publications Committee – to monitor proper accreditation and ownership of Instruct supported activities. The IP and Publications Committee shall report to the Executive Committee.
Ethics Subcommittee – to monitor implementation of the ethics policy and review issues arising. The Ethics subcommittee shall report to the Executive Committee.

7. Instruct Funding Strategy

Instruct-ERIC infrastructure will be supported primarily by Member State funding that provides a long-term foundation for Instruct. Instruct-ERIC will also seek external funding through EU and other programmes to provide funding for Instruct services.

Membership contributions: The Instruct Council will set the terms for the financial contribution of Instruct Members (Instruct-ERIC Statutes Article 13). The Instruct-ERIC annual budget will come from the contributions of Instruct-ERIC Members. A Membership commitment will be made for a 5 year period. It will consist of:
a) a cash contribution to cover the activities of the Instruct Hub and to fund Instruct activities at Instruct Centres. There will be no fee for Observers.
b) a commitment to provide infrastructure at Instruct Centres for Instruct access; where a Member hosts an Instruct Centre, it does its best to support that Centre, subject to internal review and investment procedures, to allow it to discharge its commitments as defined when appointed by the Instruct Council; these commitments will be specified in a Service Level Agreement and will include a set of rules for handling access for Instruct Users (Annex 4).

The Instruct-ERIC Funding Policy for the provision of Access is summarized in the following Table (in all cases, access is offered to Instruct infrastructure will staff support):

Category of User	Member country : research with agreement to publish	Non-Member country : research with agreement to publish – pay for service	Industrial : proprietary research – pay for service
Instrument running costs	**Paid by Instruct Centre**	Academic fee for service, subsidised by Instruct Centre	Commercial fee for service
Staff support at Centre	**Paid by Instruct Centre**		
Consumables, travel and accommodation	**Paid by central Instruct funds**	Paid by User	Paid by User
Publication of results [2]	**Yes**	**Yes**	Property of the User [2]

Instruct Members will qualify for access funded by Instruct-ERIC. Access funding will be capped at a maximum amount decided by the Instruct Council and reviewed as part of the Centres Evaluation process. Non-Members wishing to access Instruct infrastructure may apply for access based on payment of a service fee under the terms and conditions approved by Instruct Council (defined in the Access policy, Article 25 of the Instruct-ERIC Statutes). This applies to applicants from outside the Instruct Membership (including outside Europe) and to applicants from the commercial sector.

For Users from non-Instruct member countries (EU or international) Instruct will strive to allocate part of the budget to cover access costs for a number of high-level researchers , eventually through specific EU calls. The amount of access for international and non-Instruct Users will be determined by Instruct Council and will depend on funds available.

The Financial Contribution Model for Members is included in Annex 2 of the Instruct-ERIC Statutes. Instruct-ERIC will operate its principle activities on a non-economic basis.

The Instruct Expenditure Forecast Plan details the key items of forecast expenditure against the Instruct budget (based on audited financial reports from the transitional operations phase of Instruct 2012-2015). The Expenditure plan is shown in Annex 3 of this document.

External sources of Instruct funding: The Instruct Council and the Instruct Hub will explore options for external funding including grants from the EU and intergovernmental organisations, non-EU national partners, public-private partnerships and specific funded schemes for staff exchanges, technical development projects, outreach projects and sponsorships.

8. Instruct-ERIC Policies

Data Management and Biologicals Policies: These policies define a set of general principles relating to all Instruct participants and Centres and these same principles will be adopted by Instruct-ERIC. Intellectual property means property as defined in Article 2 of the Convention Establishing the World Intellectual Property Organisation, done in Stockholm on 14 July 1967. The policies include that generally open source and open access principles shall be favoured. Data acquired as a result of Instruct activity will be owned by the User(s) conducting the work. IP protection for the User will be

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[2] Article 25 of the Instruct-ERIC Statutes

the sole responsibility of the User. Where access to Instruct infrastructure is provided for collaborative projects, all Users shall agree shared ownership of data or materials prior to commencement of the work. Shared IP protection for all Users in the collaborative work will be the responsibility of the User. Specific principles shall apply to biological materials generated as a result of Instruct Centre activity and both Users and Centres should agree ownership and IP before work commences. These policy implementations will be overseen by the IP and Publications Committee. Instruct-ERIC will implement a data management plan for handling and archiving the data collected through its service provision. Particular efforts will be put into developing tools and protocols which would allow the further exploitation of the results by a broader community than the Instruct Users.

Access Policy: The Instruct Access policy is described in Article 25 of the statutes. Procedures adopted by Instruct-ERIC will be the same as those developed during Instruct implementation and described in Section 2 and more fully in Annex 1 of this document. Priority access will be given to Instruct-ERIC members. The policy will be reviewed at least 5-yearly by the Access Committee and recommendations for any amendments proposed to the Instruct Council. The ISAB may also make recommendations for amendments to the Access Policy as part of the periodic Centre review (Annex 3 to the Statutes).

Procurement policy: The Instruct-ERIC Procurement policy ensures that all tenderers are treated equally and without discrimination. The policy respects the principles of transparency, non-discrimination and competition. The Executive Committee will approve all Instruct-ERIC procurement above the value of EUR 200,000. The Instruct Director shall manage tenders following the principles of relevant EU public procurement directives and subsequent applicable national legislation. The decision to award procurement for purchases exceeding EUR200,000 shall be publicised, include a full justification and approval of the Instruct Council. VAT exemptions based on Articles 143(1)(g) and Article 151(1)(b) of Council Directive 2006/112/EC and in accordance with Articles 50 and 51 of Council Implementing Regulation (EU) No 282/2011 and on Council Directive 2008/118/CE shall apply to purchases made by and for the purpose of Instruct-ERIC (Article 24 of the Instruct-ERIC statutes).

Employment policy: Instruct-ERIC will comply with the European Charter of Researchers & The Code of Conduct for Recruitment. All Instruct Member countries have acknowledged the Charter and Code guidelines. Instruct-ERIC will ensure equal treatment and opportunities for personnel; will support mobility between Instruct Members and in general within the European Research Area and beyond; will act to attract staff in an internationally open environment. The Instruct Council shall approve the staff plan prepared by the Instruct Director and shall approve senior staff appointments and dismissals. The selection procedures for applicants will be transparent and encompass equal job opportunities, non-discriminatory and respect affirmative action policies as applicable. Where employment contracts are offered, these will follow the national laws of the country in which staff are employed.

Ethics and Governance Policy: Instruct-ERIC will implement an Ethical Governance and Framework policy that will be monitored and updated by the Instruct Executive Committee; the work will be delegated to an Ethics subcommittee as the initial referral body. The Instruct policy takes account of future strategies to build shared ELSI (Ethical, Legal and Social Implications) support services common to all the Biomedical Sciences Research Infrastructures. Instruct participated in the development of the BioMedBridges Ethical Governance policy which defines a policy bridging the Research Infrastructures (BBMRI, Elixir, EATRIS, EU-Openscreen, Euro-Bioimaging, Infrafrontier, ECRIN, EMBRC, ERINHA and Instruct). The Instruct policy takes account of national regulations and enables researchers to generate, own and access data ultimately for the purpose of advancing knowledge of the mechanisms involved in health and disease thereby benefiting society, while protecting the interests of research participants with regard to their privacy and confidentiality.

9. Instruct-ERIC Stakeholders

User groups: Instruct-ERIC will primarily serve an academic community with an interest in using structural biology infrastructure as a tool for their research. This community is made up of those who already possess some expertise in structural biology methods and wish to take advantage of the very high quality instrumentation and support provided by the Instruct infrastructure. In addition, increasingly researchers from more peripheral fields look to adopt structural methods. This is fertile ground for Instruct development with opportunities to demonstrate the power and breadth of structural biology technologies to other disciplines, to train their researchers in the application of structural biology methods and to push the technology boundaries to develop new applications and refinements in the use of the infrastructure.

Industry makes up a potentially large User group for Instruct-ERIC. Expansion of the User community into the industrial sector will be driven by the Instruct Industry Committee which will look into the best ways of providing services to industry and engaging with their existing processes. Scope exists in creating collaborative networks, training events and new research opportunities and specifically showcasing new technologies that may be transformative in certain industrial sectors and encourage their rapid uptake. Instruct has recently established a MOU with the Structural Genomics Consortium Oxford which specialises in chemical fragment screening using X-ray methods. Instruct-ERIC will support and facilitate drug discovery and development by enabling broader uptake of screens that utilise new technologies, such as higher throughput electron microscopy screening to study protein-protein and protein-drug interactions based on a synchrotron delivery model. Industry Users may access Instruct through two different routes: for pre-competitive work that allows peer review and publication of data, access can follow the academic submission route. For industry Users wishing to protect their research data, access can be provided for an agreed service fee per infrastructure platform (see Table 'The Instruct-ERIC Funding Policy for the provision of Access', Section 7 of this document). This mode of access will be governed by a User-Centre agreement with the Instruct Centre's host institution, but the process of application and User chaperone will be facilitated by Instruct. Instruct-ERIC will encourage joint development of new applications for Instruct technologies and tailored application for industrial workflows for druggable target development.

Instruct-ERIC will provide for the diversity of Users interests and needs and this will be in part enabled through Instruct's involvement with ESFRI and the other BMS research infrastructures, through the BMS Strategy Group. Instruct extends through to the IMI programme and offers its training courses through the On-Course (https://www.on-course.eu) portal which reaches 31 EU and Associated states, logging 200 users and 20 new registrations per month. Instruct-ERIC will build on these foundations to increase User diversity.

Large project consortia: As a coherent infrastructure Instruct is ideally configured to act as a resource for large projects such as those funded through Joint Programming Initiatives, large national funding initiatives and other large international consortia projects where structural approaches can strengthen research outcomes. Thus, Instruct-ERIC can provide the means to apply new and powerful methods that will achieve important results.

Other stakeholders: Other stakeholder groups are linked with Instruct and Instruct-ERIC will consolidate foundations with EU, national and intergovernmental funding bodies, policy makers, the scientific community at large, the general public. Public awareness of Instruct value and scientific impact is of key importance to Instruct-ERIC.

ANNEX 1: INSTRUCT ACCESS POLICY AND PROCEDURES

1. Statement of Principles

Instruct makes structural biology infrastructure available for access by European scientists from Instruct Member countries.

Instruct Centres commit to the provision of a stated proportion of their total infrastructure access capacity dedicated for Instruct activity. The proportion varies between Centres and is specified in the Centres Agreement drawn up between Centres and the Coordination Hub for the delivery of Instruct services. Committed Instruct capacity should be a minimum of 10% of total capacity and typically 20-30% of total infrastructure access per Centre.

The principles of access provision are the following:

- Access may be granted to any User.
- Access is made available following review of proposals primarily for scientific quality and technical feasibility.
- Access to infrastructure at Instruct Centres is provided in standard access units as published on the Instruct website.
- Use of Instruct infrastructure has expert support at the platform.
- For Users from Instruct Member countries, access to Instruct infrastructure for non-proprietary research is supported by Instruct funding.
- For Users outside Instruct Member countries, access to Instruct infrastructure for non-proprietary research incurs a charge levied by the Instruct Centre based on a published 'academic' fee per access unit.
- Users granted access for non-proprietary research must agree to publish and make publicly available data arising from the access. Users must correctly acknowledge Instruct in any publication arising from data generated as a result of access.
- For Users undertaking proprietary research, a published commercial fee for service will be levied by the Instruct Centre. Proprietary access does not require publication of the data.

Instruct access is managed through a central online portal at (http://www.structuralbiology.eu/).

The purpose of this policy is to provide Users accessing Instruct infrastructure with information and guidance on eligibility for access, the review process, the remuneration available for physical access visitors and the obligation to correctly acknowledge the infrastructure as appropriate.

2. Policy responsibility

The Instruct Executive Committee has overall responsibility for this policy and will review it at least annually.

3. Proposal Submission and Review

Application calls for access will be published at least three times per year with a defined deadline. An open access call may also be implemented.

All applications will be evaluated primarily on scientific merit; they should demonstrate innovative approaches within integrative structural biology. Proposal revision and resubmission is allowed. The aim of Instruct is to encourage the integrative use of technology and methodologies. Guidelines for applicants are provided on the Instruct website; support for applicants is available at admin@structuralbiology.eu.

4. Eligibility for Instruct access

The following user groups are eligible for Instruct access:

All Users: Any scientist proposing access to undertake good science.

Academic Users from Instruct Member countries: Access will be provided via one or more Instruct Centres to infrastructure and be financially supported with Instruct funding (covering travel, accommodation for the User and limited funding for consumables for the Instruct Centre providing the access). The limits of Instruct funding available will be published on the website. Access is granted on condition of data being made publicly available and proper acknowledgement of Instruct.

Academic Users from non-Instruct Member countries: Access will be provided via one or more Instruct Centres to infrastructure subject to a service fee at a published academic rate being charged by the Instruct Centre for each access unit. Access is granted on condition of data being made publicly available and proper acknowledgement of Instruct.

Commercial Users: Scientists from commercial organisations may apply through two different routes:

Commercial scientists doing non-proprietary research: Any scientist from a commercial pharmaceutical or biotechnology company from a member state can apply. Access is granted for work using the same rules as for academic users. The proposers must agree to publication of data (a publication delay can be negotiated to allow IP and patent processes). Access is granted on condition of data being made publicly available and proper acknowledgement of Instruct.

Commercial scientists doing proprietary research or requiring a service provision: Access may be granted subject to the following: i) A commercial access service fee will be charged per access unit; ii) IP issues will be agreed before commencement of the access. Commercial access will not require data to be made publicly available.

5. Publication of research:

Instruct has a policy to publish data arising from research undertaken using Instruct infrastructure in peer reviewed journals. Publication should include an acknowledgment of Instruct: "The authors acknowledge the support of employees and the use of experimental resources of Instruct".

Users are required to submit to the Instruct Hub an experimental report generated as a result of the use of Instruct facilities no later than twelve (12) months after the visit. Within thirty (30) days of publication, users should notify Instruct of the title, authors and date of any scientific publications or papers published as a result of Instruct access. Access to further Instruct Centre infrastructure may be affected if users do not comply with this requirement.

6. Proposal review

Academic users and Commercial users submitting proposals for precompetitive research will be subject to the scientific review process. Proposal information will be shared with external experts to review applications.

Moderators will assess proposals according to the following initial criteria:

Eligibility for Instruct funding support: Proposals must originate from an Instruct member country.

Field of research and request for platform access: The research should fall within the broad field of structural cell biology and be well matched to the infrastructure provided through Instruct.

Three reviewers will be appointed for each proposal; one internal reviewer and two external reviewers. The Moderator may return comments to the User on the proposal outcome including advice on next steps. The proposer will receive all three anonymised reviewers' comments, their scores and the Moderator's comments.

Moderators and Reviewers will be bound by a confidentiality agreement not to disclose or otherwise exploit any information that is provided as part of the access application.

Appeals: An applicant has the right to appeal the outcome of the review process. The Moderator will manage this process according to the guidelines published on the website.

Proposals approved by the Review Panel will undergo a Technical Review by the Instruct Centre to check on feasibility of the proposed work and capacity of the Centre to deliver the access requested. The Instruct Centre will advise on the number of access units appropriate for the scale of the work proposed.

Commercial Service Access proposals will not be subject to review. However proposals will undergo a Technical review by an Instruct Centre as above.

7. Costs of access covered for Instruct member users

The complete model for Access funding includes the following components:

The cost of providing the infrastructure, its maintenance, instrument running costs, support staff and nominated consumables costs for the access projects will be funded through the member country 'in-kind' contribution to Instruct Centre (the "Facility Cost"). The value of this contribution per access unit will be quantified by the Centre.

Travel and accommodation for Access will be reimbursed from Instruct funds administered through the Instruct Hub (the "Support Cost"). The Support Cost per access visit will be capped and the amount published on the website.

Instruct Centres will publish their unit costs for provision of access on the Instruct website. The Centres will advise on the number of access units appropriate for each access visit, where each visit may be allocated a support cost allowance for travel and accommodation (see above).

Where consumable costs for access significantly exceed the unit cost as published, these costs will be agreed between the Centre and the User before the work is undertaken, and a mechanism to cover these costs will also be agreed. This may include an additional contribution from the User towards the extra consumable costs.

8. Terms and Conditions for Instruct Centres: User access

Users are required to comply with Instruct Centre health and safety rules, policies and procedures. The Instruct Centres are responsible for ensuring compliance.

Users will notify Instruct prior to publicizing any part of the work conducted at Instruct Centres.

Intellectual property issues will be agreed before commencement of access at each Instruct Centre.

Limitation of liabilities will be explained and agreed before commencement of access at each Instruct Centre.

Users shall at all times comply with all applicable laws, regulations and guidelines at each Instruct Centre.

The use of facilities at Instruct Centres is deemed as acceptance of these Terms and Conditions, sight of which should be made available to all users attending Instruct Centres for access.

ANNEX 2: EXPENDITURE PLAN

Instruct Income/Expenditure forecast August 2016 - July 2020 (€s)	y1 2016	y2 2017	y3 2018	y4 2019	y5 2020
	€	€	€	€	€
Income					
Membership Income (15 members)	900,000	918,000	936,360	955,090	974,190
Income from grants	168,187	168,187	168,187	270,842	176,060
sponsorship raised for Biennial conference	40,000	-	40,000	-	40,000
Total Income	1,108,187	1,086,187	1,144,547	1,225,932	1,190,250
Expenditure					
Staff Costs	204,000	304,000	310,080	316,282	322,607
UOXF financial management services	42,000	42,840	43,697	44,571	45,462
Hub running costs	49,574	50,000	51,000	52,020	53,060
Legal and Audit Fees	5,000	5,000	5,000	5,000	5,000
Travel; meetings; Biennial	29,074	90,000	30,000	90,000	30,000
Total Hub	329,648	491,840	439,777	507,872	456,130
Access	438,539	254,347	364,770	378,060	394,120
Training courses, grants	130,000	130,000	130,000	130,000	130,000
R & D Grants (0)	100,000	100,000	100,000	100,000	100,000
Internships	30,000	30,000	30,000	30,000	30,000
Travel to Science Meetings and Conferences	80,000	80,000	80,000	80,000	80,000
Total Instruct activities	778,539	594,347	704,770	718,060	734,120
Total Expenditure	1,108,187	1,086,187	1,144,547	1,225,932	1,190,250

*subject to renewal of EU grants; ^ increased on senior appointment in 2017; † Biennial costs in 2017 & 2019

ANNEX 3: SERVICE LEVEL AGREEMENT BETWEEN INSTRUCT-ERIC AND INSTRUCT CENTRE

Instruct Service Level Agreement between [Institution hosting the Instruct Centre]

and Instruct-ERIC

For

The Instruct Centre provision of Structural Biology Research Infrastructure Access to Instruct-ERIC

THIS AGREEMENT is made the   ………….   day of   ………………. 2016

BETWEEN

1.   **Instruct-ERIC (offices at the Wellcome Trust Centre for Human Genetics, Roosevelt Drive, Oxford, United Kingdom)**

AND

2.   **INSTITUTION (XXX)**

BACKGROUND

   A. Instruct means the Integrated Structural Biology Research Infrastructure set up as part of the ESFRI Roadmap and, from the date of the Commission Establishing Decision establishing Instruct-ERIC, coordinated by Instruct-ERIC;

   B. Instruct provides access to research infrastructures through Instruct Centres, which are the sites at which Instruct related activities are carried out, as defined in the statutes of Instruct ERIC;

   C. New and existing Instruct Centres shall be selected and periodically evaluated by the criteria laid down by the Instruct Council and detailed in Annex 3 (relating to Article 15) of the Instruct-ERIC Statutes;

   D. Instruct-ERIC Members will do their best to provide the Instruct Centre in their territory with the most appropriate resources for the activities of the Instruct-ERIC and do their best to provide access to the Centres, as defined in Instruct-ERIC statutes;

   E. The "Instruct Service Level Agreement" is the instrument referred in the statutes of Instruct-ERIC regulating the provision of Instruct access, training and any other Instruct activity offered by the Centre; the responsibilities of the Centre in its service and adherence to Instruct policies as applicable, as defined in the statutes of Instruct-ERIC.

IT IS AGREED AS FOLLOWS:

INSTRUCT-RELATED FACILITIES AND FUNDING

An Instruct Centre will make available its Instruct-related facilities for the performance of Instruct. The capacity of access pledged by a Centre for Instruct-related access is detailed in an Annex to this agreement. The priorities and allocation of the actual use of its Instruct-related facilities is at the Centre's sole discretion.

Prospective changes to the Instruct-related facilities specified in annex 1 should be notified to the Instruct Executive Committee. Substantial changes shall be evaluated against the Centre criteria to ensure continued quality of service provision by the Centre.

The funding model for delivery of access by Instruct-related facilities is defined in the Access Policy (Article 25 of Instruct-ERIC statutes) and can be viewed in the online Instruct catalogue. For informative purposes only, the Centre will also provide an estimation of the total cost of Instruct-related facilities and a service fee for non-Member Users.

A Centre will advise Instruct-ERIC as soon as possible of significant down time of any of its Instruct-related facilities due to repairs or routine maintenance.

A Centre will advise Instruct-ERIC of any significant proposed or actual upgrades to any of its Instruct-related facilities.

If a Centre acquires any new equipment relevant to Instruct, it will at its discretion add this equipment, or a fraction of it, to its list of Instruct-related facilities. This would be expected if funding came as a result of the centre having Instruct status.

USERS

The Centre will provide any basic training it deems necessary in the use of any of the Instruct-related facilities which the User is authorised to use as part of the research programme.

The Centre may, by agreement with the User and at the User's expense, provide additional training.

Agreement by a Centre to provide infrastructure access to a User will require at least the following commitments on the part of the User:

- o to comply with the Instruct Centre IP, Data and Biological policy, as approved and kept updated by the Executive Committee, and made public on the Instruct Web site.
- o to comply with the Instruct branding guidelines as approved by the Executive Committee;
- o agreement by the User to obtain all necessary consents and to comply with all relevant ethical guidance, and to provide sufficient information to the Centre to allow a full and proper evaluation of safety and ethical risks by the Centre;
- o to ensure that it will comply with the Centre's rules and regulations on the use of the Centre's computer network and with the Centre's health and safety policies and procedures whilst on the Centre's premises. Users shall be responsible for any loss, damage or injury as a result of the User's failure to comply with the Centre's Health & Safety policies and procedures and shall indemnify the Centre and keep it fully and effectively indemnified against any and all losses, costs (including professional fees) and liabilities which may accrue to the Centre as a result of any breach of its obligations.
- o to adhere to the principle of publishing and making publicly available the data arising from access in order to qualify for Instruct funding.

Users will be required to agree these commitments before access is delivered. The Centre will report to the Instruct Hub any breaches by a User of its agreement, or any misuse of the Instruct-Related Facilities.

CENTRES' RESPONSIBILITIES

The Centre will ensure that any work it carries out in furtherance of Instruct's objectives is in accordance with the terms and conditions of its funding and that it complies fully with all applicable laws, regulations and guidelines, in particular including those governing health and safety, data protection, and where relevant, the use of human or animal subjects and good clinical practice. In particular:

The Centre will ensure that full confidentiality or anonymity is maintained for all samples and data relating to the use of human subjects which are generated using facilities accessed through Instruct;

The Centre will verify that the User has obtained all necessary approvals from the relevant bodies and provided sufficient information relating to the intended research for the Centre to assess issues of ethics and safety related to the access;

The Centre will comply with the Instruct branding guidelines;

The Centre will comply with the Instruct IP, Confidentiality and Publications policies, to be kept updated by the Executive Committee, approved by the Instruct Council and made public on the Instruct Web site; and

The Centre will report annually to the Instruct Hub to include the metrics requested by the Instruct Council.

PARTICIPATION IN INSTRUCT

The Centre shall appoint an Instruct Centre Coordinator or Coordinators who will be responsible for liaison with the Instruct Hub. The Centre will supply the Instruct Hub with the names and contact details of the Instruct Centre Coordinators at the time the appointment is made, and will promptly notify the Instruct Hub of any change of Instruct Centre Coordinators.

The Centre will cooperate with the Instruct Council and with the Executive Committee where necessary in furthering the aims of Instruct.

INSTRUCT HUB'S RESPONSIBILITIES

The Instruct Hub will liaise with the Centre in all requests for the use of all or any part of the Centre's Instruct-related Facilities which have been approved by the Access Committee.

The Instruct Hub will help with scheduling between competing requests for use of the same Instruct-Related Facilities, having due regard to the freedom of each Centre to optimize their provision.

The Instruct Hub will facilitate User access to the Centre's Instruct-Related Facilities.

The Instruct Hub will deal with complaints about Users made by the Centre.

The Instruct Hub will provide the Centre with information about funding available to the Centre as a part of Instruct and will facilitate applications by the Centre for such funding.

The Instruct Hub will collate Instruct metrics regarding delivery of services to Users according to the wishes of the Instruct Council.

PUBLICATIONS POLICY

Users are expected to make every effort to publish their data with all contributions to the research acknowledged in the proper manner as made explicit on the Instruct website. All Users publishing non-proprietary work should acknowledge the Instruct Centre involved, specifically acknowledging the support of employees and the use of experimental resources of Instruct-ERIC.

TERMINATION

Proposed termination of this agreement by a Centre, either linked to Instruct Membership withdrawal (Instruct-ERIC Statutes Article 8) or withdrawal of the Centre or a facility from Instruct-

ERIC for other reasons should be notified to the Instruct Council in writing. The Instruct Council will determine the appropriate course of action which may include the re-evaluation of the Centre.

NOTICES

The Instruct Hub's representative for the purpose of receiving payments, reports and other notices shall until further notice be:

> The Hub Coordinator, Instruct-ERIC

The Centre's representative for the purpose of receiving invoices, reports and other notices shall until further notice be:

> [name of Centre representative here]

GENERAL

Clause headings are inserted in this Agreement for convenience only, and they shall not be taken into account in the interpretation of this Agreement.

If the performance by either party of any of its obligations under this Agreement (other than an obligation to make payment) shall be prevented by circumstances beyond its reasonable control, then such party shall be excused from performance of that obligation for the duration of the relevant event.

No one except a party to this Agreement has any right to prevent the amendment of this Agreement or its termination; and no one except a party may enforce any benefit conferred by this Agreement, unless this Agreement expressly provides otherwise.

Nothing in this Agreement shall create, imply or evidence any partnership or joint venture between the Instruct Hub and the Centre or the relationship between them of principal and agent.

Neither party shall use the name or any trademark or logo of the other in any press release or product advertising, or for any other commercial purpose, without the prior written consent of the other.

In case of inconsistency between any provision of this Agreement and the provisions of the statutes of Instruct-ERIC, the latter shall prevail.

This Agreement constitutes the entire agreement between the parties. Any variation shall be in writing and signed by authorised signatories for both parties.

Any disputes shall be referred to the Instruct Council to be resolved. In the event that a resolution cannot be reached, the courts of the host country shall have exclusive jurisdiction to deal with any dispute which may arise out of or in connection with this Agreement.

This Agreement may be executed in any number of counterparts, each of which when executed will constitute an original of this Agreement, but all counterparts will together constitute the same agreement. No counterpart will be effective until each Party has executed at least one counterpart.