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| **TOPIC** | **SAMPLE SERVICE** | |
| **Work packages involved** | **5** | **Chemical Deuteration – DEUNET** |
|  | **6** | **Macromolecular Crystallogenesis** |

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| **Topic objectives**  This topic focuses on two aspects of sample preparation in key areas of neutron science. The first concerns the development of a trans-European capability for the deuteration of molecules for neutron studies in the growing field of soft condensed matter, which uses a wide range of techniques for cutting-edge studies of surfaces, structures over many length scales and dynamics. The second concerns the development of new approaches to deal with a critically important bottleneck in neutron structural biology – large crystal growth. Neutron protein crystallography is starting to provide exciting new information revealing a world of detail beyond that visible with X-rays, including vital information on hydration, protonation states, protein-drug interactions, charge transport, etc. In both cases the common driver is obvious: with a wide range of advanced and expensive neutron facilities and instruments either in place or under development across Europe, and the advent of the ESS on the horizon, it is of crucial importance that strong emphasis is placed on key issues for sample preparation that will maximise the quality and impact of current and future research in these areas. |

**Table 3.1a.5: Work package descriptions**

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| Work package number | **5** | | Start date or starting event: | | | | **M3** | |
| Work package title | **Sample - Chemical Deuteration – DEUNET** | | | | | | | |
| Activity Type | **RTD** | | | | | | | |
| Participant number | **2** | **1** | | **3** | **6** | **NA** | |  |
| Participant short name | **ESS** | **ILL** | | **STFC** | **FZJ** | **ANSTO** | |  |
| Person-months per participant: | **48** | **36** | | **24** | **18** | **0** | |  |

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| **Objectives**  With the recent advances in neutron sources and instrumentation, and the start-up of ESS, there is an urgent need for deuterating complex molecular architectures for studying a range of advanced materials with neutron scattering. DEUNET will address the issue by developing:   * **A cost-effective platform** to provide access to a broad range of materials and expertise * **New synthetic** methods and products * **Synthesis of innovative materials** in collaboration with partners * **Coordinated service** for European neutron users   Per-deuterated materials are rarely available from commercial suppliers except through costly custom synthesis, and due to the small scale (mg-g) and large variety of deuterated compounds required by a comparatively small market they will continue to be of very limited interest to the chemicals industry. The Oxford Isotope Unit has been providing a selection of simple compounds obtained primarily by catalytic H-D exchange while ILL has pioneered biological deuteration of proteins, but more complex small molecules are not available to the community today. This limits the experiments that can be performed, and forms a bottle-neck for advancing the applications of neutron scattering. The situation is particularly problematic for novel materials with potential industrial applications in (bio)nanotechnology, electronic devices and biomedicine, as new molecules are constantly produced in the race for improved performance, efficiency and cost. Many of the deuterated compounds purchased commercially are prohibitively expensive and could be produced at a fraction of the cost in optimized laboratories. The development of new synthesis, purification methods and materials forms the foundation for leveraging the full potential of the ESS, particularly in the areas of soft condensed matter, functional materials and the biomedical sciences. The European neutron user community also does not have uniform access to deuteration services, and providing this will be a key step in maximizing the scientific impact of all European neutron facilities.  To broaden the range of compounds available, and to provide a cost-effective service and coordinated user access, we propose to establish a European platform for chemical deuteration (DEUNET) in the form of a network between the ESS, ILL, STFC, and FZJ. A node for advanced molecular synthesis at ESS, and the long-standing experience in polymer synthesis at FZJ will complement the core capabilities of the existing deuteration laboratories at ILL and ISIS. We will also benefit from the experiences gained at the Australian National Deuteration Facility at ANSTO through their participation in DEUNET as an observer. The platform will maximize the benefits from the extended capabilities by using the complementary expertise of the partners to achieve the most cost-effective syntheses and to develop synthetic routes for a broad range of compounds, as well as by sharing and recycling deuterated raw materials where possible. During SINE2020, particular attention will be paid to consulting the user community about the requirements for the services, establishment of a user access portal, and cross-fertilisation of ideas through collaborations and staff visits between the facilities.  While the four facilities will act as the core of the platform through which the activities are coordinated and carried out, we will also involve external groups to enhance the knowledge base and synthesis available for applications requiring specialized equipment. The platform will operate and provide user access on a collaborative basis during this project, with the goal beyond SINE2020 being to provide transnational access to the service as well as to extend the collaboration internationally.  A significant fraction of the materials that will be synthezised within the platform have industrial applications or recognized innovation potential, and chemical deuteration is of crucial importance for understanding function and improving the efficiency through detailed neutron scattering studies. For example lipids, oils and biosurfactants derived from microbial biomass are of current topical interest for developing better industrial enzymes, drug delivery systems and biodegradable emulsions and detergents. Both biological and synthetic polymers have a wide range of industrial applications from elastomers and adhesives to additives in cleaning products. Neutron scattering also lends itself ideally to *in situ* studies of processing techniques involved in manufacturing of products. Although strong collaborations are already in place between the large facilities involved and health/home care companies, as well as SMEs involved in drug development/biomaterials, we will develop outreach material for industry in collaboration with WP4 to promote the benefits of deuterium labeling. |

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| **Description of work**  **Task 5.1. Chemical deuteration by catalytic H-D exchange and synthesis of surfactants (ISIS)**  Currently the ISIS isotope facility provides a base of deuterated materials for the UK neutron scattering community. Under this project the provision will be extended to the European user community and a broader range of compounds will be synthesized in collaboration with the partner institutions. At present, the compounds available at ISIS are deuterated aliphatic hydrocarbons, such as fatty acids, alkanols and a selection of their derivatives including surfactants. A range of other compounds can be synthesized on request and there are already a number of priorities for new compounds including oleic acid and non-ionic surfactants with deuterated headgroups.  **The main tasks carried out at ISIS will be:**   * ***Provision of starting materials*** to the other partners to enable the synthesis of compounds currently unavailable, for example polymers and selectively labelled lipids (D5.1, 5.5) * ***Expanding access*** to the existing compounds for ***European (non UK) researchers*** (D5.7) * Improved syntheses for the production of deuterated ***unsaturated fatty acids*** *(D5.7, D5.11)* * ***Development of routes to novel bio-surfactants*** in collaboration with ILL and ESS (D5.11).   Within these tasks the post-doctoral researcher recruited will receive training and support from the existing isotope facility staff. A number chemical analysis tools are available at ISIS (light scattering, surface tension, IR, mass spectrometry etc.) and at the Research Complex at Harwell (NMR, chromatography).  **Task 5.2. Extraction and purification of small molecules from deuterated cell cultures (ILL)**  Currently the ILL D-lab, specialized in macromolecular deuteration, provides ILL users with deuterated proteins and biomass for extraction of other compounds, such as DNA. Within this network, we will set-up, in the framework of the Partnership for Soft Condensed Matter (PSCM), procedures for the separation, purification and analysis of small, deuterated biological molecules derived from cell cultures, which will complement the macromolecular deuteration capabilities. The main task will be to develop methods for the ***separation and purification*** of:   * Main amphiphilic lipid components of biological membranes * Raft forming molecules such as gangliosides and cholesterol * Polysaccharides   This will include optimization of procedures for the production, partial labeling and purification; lipid separation; polysaccharide fractionation (D5.9) and analysis using tools available on the EPN campus (D5.10) including IR spectroscopies, size exclusion chromatography, NMR, mass spectroscopy, light scattering, neutron and x-ray scattering. Relevant molecules, such as biological sugars and lipid headgroups, will be shared with the other partners of the platform or users for chemical modification and partial labeling of molecules.  **Task 5.3. Synthesis of complex deuterated molecules (ESS)**  The ESS node (DEULAB) will focus on the ***chemical synthesis of complex deuterated molecules*** based on both biological and non-biological starting materials, and on developing ***novel deuteration methods***. Some of the key compounds that are urgently required include:   * chiral, cyclic and unsaturated compounds * compounds synthesized from natural components such as sugars and lipids * monomers for polymer synthesis, polymer-modified lipids   Two PDRA’s will be recruited to i) develop a range of methods for chemical reactions using deuterated materials, and ii) synthesize a selection of labelled compounds in collaboration with ISIS, ILL and FZJ (D5.11). In particular, the ESS will develop the ***enzyme-catalysed synthesis*** of chiral deuterated compounds, such as L- and D-lactic acid (D5.4), which will be applicable to many other cell-free syntheses of biomolecules. Polylactic acid polymers (biodegradable plastics) will be polymerised at FZJ (D5.8). In addition, both ESS PDRAs will contribute 25% of their time to the establishment of the DEUNET platform (Task 5 and D5.1, D5.6, D5.12).  **Task 5.4. Polymer synthesis (FZJ)**  The Jülich lab has a broad experience in the synthesis of ***homopolymers, block copolymers and branched architectures*** in partially or fully deuteratedforms. These can be on the basis of some commercially available deuterated monomers like styrene, butadiene or ethylene oxide, or in collaboration with ISIS where the deuterated alkyl precursors for the monomers are available. In the framework of the platform, the Jülich lab will develop ***new synthesis procedures*** for deuterated monomers and polymers of topical interest that cannot be obtained via commercial suppliers, including isoprene (D5.3), the basis of natural and synthetic rubbers, and polythiophenes, which are of high relevance for photovoltaic or LED applications. We will devise synthesis routes for thiophene-based labelled monomers in collaboration with ISIS (D5.5). The technologies for the synthesis of the polymers are already established in our lab. In addition, FZJ will collaborate with ESS in the synthesis of polymer modification of lipids (PEGylated lipids) (D5.11) for biomedical applications and in the synthesis of biodegradable polymers based on polylactic acids (D5.8), for which the enantiomerically pure L- and D- lactic acid monomers are synthesised at ESS (D5.4).  **Task 5.5. Network coordination and platform activities (ESS)**  The ESS node will coordinate the WPactivities and the establishment of the platform, in particular we will:   * Organise the networking events, annual meetings and dissemination of results * Organise a User workshop to define scope and strategy for DEUNET (D5.6) * Set up a network of collaboration network (neutron facilities, university laboratories, user organisations) * Coordinate the establishment of the platform management, operation and access (D5.12) * In collaboration with WP2 (Dissemination), set up a webpage and user portal (D5.1) * In collaboration with WP3 (e-learning), provision of e-learning material about deuterium labelling * In collaboration with WP4 (Industry), develop industry-specific outreach material |

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| **Deliverables**  **Task 5.1 (ISIS)**  D5.2 Synthesis of precursors to surfactants, lipids and polymers (M12) R, CO  D5.7 Synthesis of deuterated surfactants for European users (M28) R, DEM, PU  **Task 5.2 (ILL)**  D5.9 Optimization of techniques for separation and purification methods (M36) R, DEM, PU  D5.10 Physico-chemical characterization of purified biomolecules (M42) R, PU  **Task 5.3 (ESS)**  D5.4 Synthesis of L- and D-lactic acid (M18) R, DEM, PU  D5.11 Synthesis of novel deuterated lipids and surfactants (M42) R, DEM, PU  **Task 5.4 (FZJ)**  D5.3 Novel route for isoprene synthesis (M15) R, PU  D5.5 Synthesis of deuterium labelled polythiophene based block copolymers (M20) R, PU  D5.8 Synthesis of deuterium labelled polylactic acid (M30) R, PU  **Task 5.5 (ESS)**  D5.1 Webpage and user portal established for DEUNET (M9) DEC, PU  D5.6 Report on the scientific impact and requirements for chemical deuteration in Europe(M24),PU  D5.12 DEUNET Platform management, operation and user access scheme (report)(48) R, PU |