D2.1 Improved protocols for compound sourcing and acquisition based on EU-OS Ambassador feedback, including a directory of cooperating chemists from each country

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1 Introduction

The EU-OPENSCREEN (EU-OS) compound collection is composed of two parts:

- a collection of 100,000 commercially available compounds from various vendors, identified using tailored cheminformatics algorithms developed during the preparatory phase,[1] and
- a collection of academic compounds, crowd-sourced from European chemists.

The collection of this academic part will add substantial uniqueness to the EU-OS compound collection and realize the vision of a truly European Compound Collection covering unbiased chemical diversity with an expected size of 140.000 compounds (100.000 commercial and 40.000 academic compounds).
The WP2 in EU-OPENSCREEN-DRIVE, "Academic Compound Acquisition", focuses first of all on establishing a legal framework as well as the whole compound donation, registration and handling process required for collecting the compounds from chemists.
In the next phase, our aim is to raise awareness among the chemistry community of the benefits of donating compounds to EU-OS, informing chemists about the legal aspects and offering them practical guidance. Initially, we will directly engage with the first generation of compound providing users in at least eight European countries with the aim to collect up to 10,000 compounds from approximately 100 chemists.
In more detail, the main objectives of WP2 are

1. enabling effective and coordinated flow of compounds from academia into EU-OS´s joint compound collection;
2. ensuring that data associated with the academic compound collection and integration into the EU-OS library is compliant with "FAIR" principles (Findability, Accessibility, Interoperability, and Reusability);
3. increasing chemists' awareness of the EU-OS compound collection in member and observer countries;
4. generating trust among the chemists by clear communication of benefits accruable to them, their institutes, and for society, as well as legal aspects, rights and responsibilities, and
5. guiding the chemists in the selection process, preparation and submission of their compounds by means of the online compound registration portal.

[1] Horvath, D., Lisurek, M., Rupp, B., et al. Design of a General-Purpose European Compound Screening Library for EU-OPENSCREEN, *ChemMedChem* **2014**, *9*, 2309–2326.

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This deliverable D2.1 'Improved protocols for compound sourcing and acquisition based on EU-OS Ambassador feedback, including a directory of cooperating chemists from each country` relates to task 2.1 'Develop a protocol to acquire compounds from European countries in a coordinated and organized way' and tackles some aspects of task 2.2. 'Implement and pilot test a software solution for managing the federated compound acquisition procedure' of WP2. Those are ongoing tasks foreseen to end in Month 18. Therefore, this deliverable summarizes the results of the work performed during the first 12 months of the EU-OPENSCREEN-DRIVE project, while sourcing and compound acquisition will be continued.

2 Discussion

2.1 Protocol for compound sourcing and acquisition

In order to meet WP2 objectives, in the beginning of the project, we first established an "Academic Library Working Group" (referred to as working group), consisting of "EU-OS Ambassadors" from ERIC member countries, who solicit compound donations from their national scientific communities and drive the crowd sourcing process through local contacts and building trust with donors. The composition of this Working Group is the following:

CZ: Martin Popr, IMG
DE: Marc Nazaré, FMP
DK: Mads Hartvig Clausen, DTU
ES: Mabel Loza, USC
FI: Päivi Tammela, UH
LV: Aigars Jirgensons, OSI
NO: Johannes Landskron, UiO
PL: Zbigniew J. Lesnikowski and Agnieszka Olejniczak, IMB
ERIC office: Edgar Specker

Together with the EU-OS central office, the working group developed a legal framework to support the process of federated acquisition by preparing the first draft of the Material Transfer Agreement (MTA) based on similar national agreements. This MTA shall be used for collecting compounds from academic chemistry groups. The conditions and procedures related to the MTA have been discussed in several telephone conferences held in 2019 and the donation process described in the MTA was coordinated with the ambassadors in the WP2 workshop organised in Madrid on April 3, 2019. During the workshop, the EU-OS ambassadors briefly presented the current national practices in each ERIC country, and these experiences were funnelled into the process for collecting academic compounds for the EU-OPENSCREEN compound collection.
After the work done by the working group, the MTA was opened for comments to the whole EU-OS network, reviewed by several legal consults at partner universities and finalised.
Figure 1 shows the established process workflow for the academic compound collection. At first, the chemist needs to provide 10 mg (or at least 5 mg) of each compound with a purity of >90 %. Furthermore, the compounds are evaluated by reactivity rules in order to flag these compounds as potentially reactive compounds or promiscuous binders. As EU-OS strives for a structurally diverse library containing compounds with highly attractive scaffolds, the diversity profile of the donated library will be checked as well.

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If the EU-OS Central Compound Management Facility (CCMF) confirms that the purity of the compound is >90%, the compound will be integrated in the EU-OS compound collection. The academic compounds will be comprehensively characterised in a bioprofiling process. The aim is to analyse these compounds based on their physicochemical and toxicological properties. This data will serve as selection criteria for hits in the subsequent assay campaigns conducted at the different Screening Partner Sites (SPS) of EU-OS. For example, a set of compounds might only interfere with assays based on fluorescence read out, others are prone to interact specifically with a technology, or toxic compounds might disturb the signal in cell-based assays. Finally, the bioprofiling data will be deposited in the EU-OS'S European Chemical Biology Database (ECBD) in a non-disclosed section with an embargo time of 6 months allowing the chemist to exploit the data for publication. Afterwards, the data will be made publicly accessible in the ECBD.

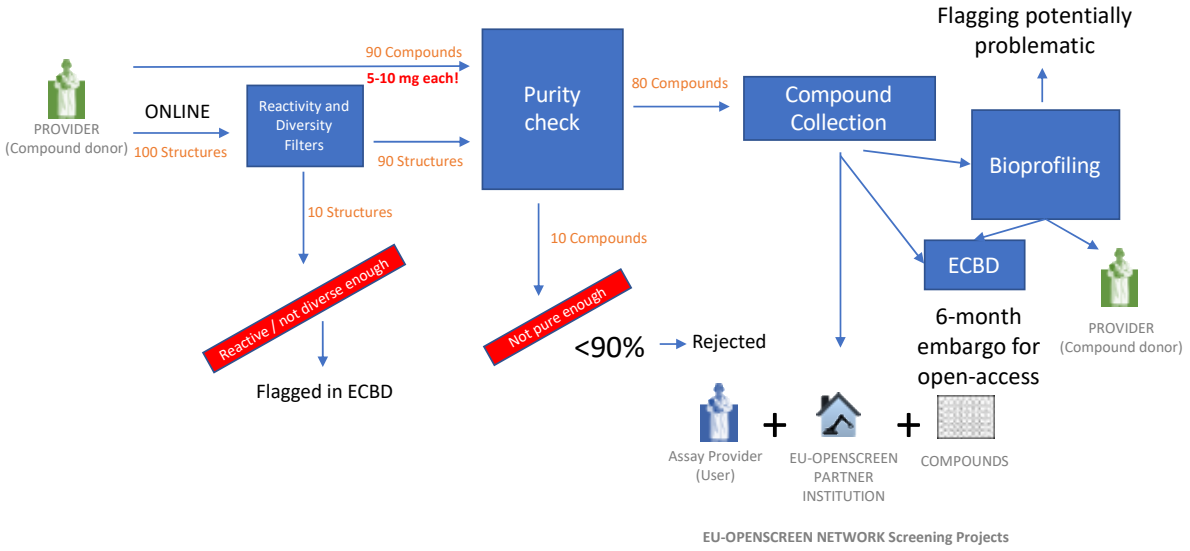

Figure 1: Process workflow for collecting academic compounds

Once the academic compounds are in the EU-OS compound collection, they shall be distributed by the EU-OS ERIC CCMF to the EU-OS SPS. At the partner site, the academic compounds will be made available to users, in the context of user-initiated screening projects. If a bioactive compound with validated activity is discovered within such project, the following process is described in Figure 2. This process aims at establishing new collaborative projects based on the discovered bioactivity between compound-donating chemists and users, and it will be supported by EU-OS Screening and Medicinal Chemistry Partner Sites as needed.

In fact, if a compound is identified as a validated hit in a screening campaign with a confirmed biological activity, validated by a concentration response curve and usually expressed as an EC50 (for stabilizers and activators) or an IC50 (for inhibitors) value, accompanied with lack of activity in a counter screen, the data is uploaded in the non-disclosed section of the ECBD for an embargo time of 6 months. The provider and user are simultaneously informed via an automated notification system about the validated hit in order to facilitate the connection between provider and user to trigger further collaboration. If both parties agree to collaborate they can decide for an additional embargo time of 3 years starting from the upload of the data to the non-disclosed section of ECBD where they will be stored until the end of the embargo time. After the embargo time the data will be made publicly available in the ECBD.

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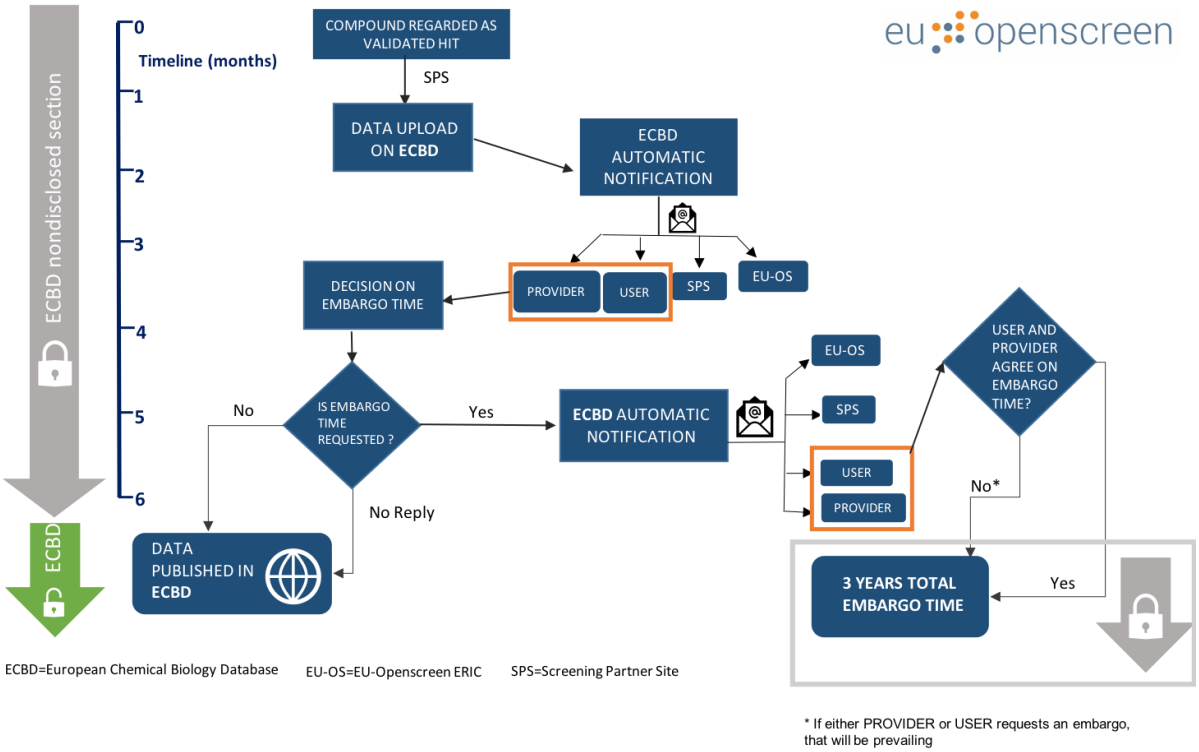

Figure 2: Process workflow after a bioactive compound have been identified from academic compound collection in a screening project.

However, the chemist or the user may express a written refusal to collaborate with each other or one of the parties may give a written permission to the other party to continue the research on the validated hit on its own or with a third party. If one of the parties does not give its permission, the other party is not allowed to use their corresponding data.
These processes and related conditions are described and regulated within the MTA.

2.2 Software solution for managing the federated compound acquisition procedure

As next steps in this WP, our aim is to establish the required platforms for the compound collection, such as an electronic compound submission system. Chemists will be able to submit the drawn structure, their corresponding IDs and the amount of donated compound via a web portal. An example of such a software tool is shown in Figure 3.
An electronic compound submission system facilitates the submission of electronic data on the compound structure, amount of material and the vial identity code. This IT solution will ensure that each sample can be correctly identified, tracked and linked to the donating chemist by applying unique identifier codes. We will store the academic library in 24-well plate format filled with tubes containing a 2D barcode on the bottom and a 1D barcode on the side of each tube. The software has to be adapted to this 24-well plate format and the barcodes of the tubes will be included in the electronic submission system. As soon as the chemists have electronically submitted the compounds, the data will be processed within the ERIC and will be cross-checked with the chemists (structure correctly drawn, vendor Comp_ID correct *etc*).

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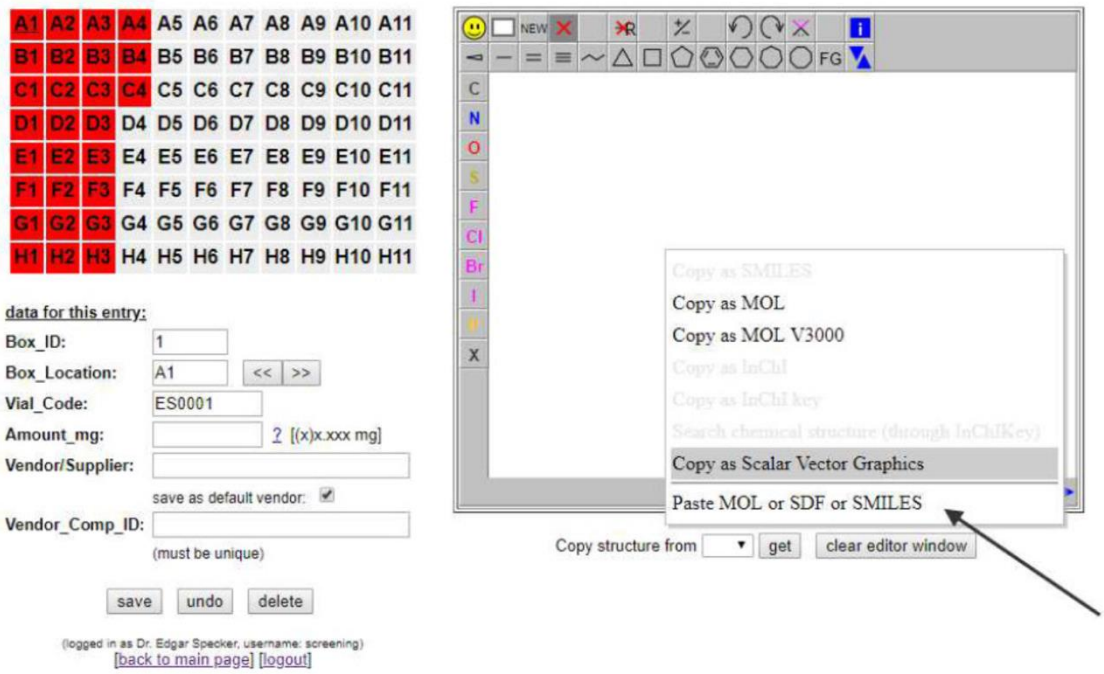

Figure 3: Example of a webportal for electronic submission of compounds.

As soon as we approach the chemists via different channels (email, conferences, oral communications, *etc*), we will provide them with the MTA, a cover letter explaining and summarizing the key messages of the MTA, an account for the web portal together with a short manual on how to use it. Additionally, we will implement an option that would allow chemists to express their interest in compound donation and send the information request electronically through an on-line platform available at the EU-OS website. All potential donating chemists' names will be gathered in a dedicated directory to facilitate the acquisition campaign and compound sourcing by the EU-OS Ambassadors (GDPR compliance will be strictly followed).

2.3 Conclusions

Summarising, within deliverable D2.1 we have established standardized protocols for sourcing and acquisition of academic compounds that will be integrated into the EU-OPENSCREEN's compound collection. This was achieved through the work of dedicated EU-OS Ambassadors in every ERIC member country gathered together in an 'Academic Library Working Group'. The working group together with the EU-OS central office developed a legal framework to support the process of federated acquisition. A continuous engagement of the EU-OS Ambassadors will lead to the construction of a directory of cooperating chemists and to the establishment of procedural tools to support the compound acquisition process.

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