



D4.1

FBDD chemical evolution consultation service guidelines

Version 1.0 2020-01-31

for

H2020-INFRADEV-2018-1

(Development and long-term sustainability of new pan-European research infrastructures)

Research and Innovation Action (RIA)

Action Acronym:

EU-OPENSSCREEN-DRIVE

Action Full Title:

“Ensuring long-term sustainability of excellence in chemical biology
within Europe and beyond”

Grant Agreement No.: 823893

Dissemination level: public

Document Properties:

Deliverable	D4.1: FBDD chemical evolution consultation service guidelines
Partner responsible	OSI, HZI
Author(s)	Aigars Jirgensons (OSI), Mark Brönstrup (HZI), Tanja Miletic (EU-OS), Katja Herzog (EU-OS)

1 Aim of the guidelines

Fragment hit-to-lead development requires collaborative efforts of biophysical chemistry, structural biology, medicinal chemistry, and disease biology. Research groups performing the fragment library screening often lack in house expertise of further chemical evolution of the fragment hits and would benefit from an assistance from medicinal chemistry groups. These guidelines provide EU-OPENSSCREEN (EU-OS) fragment library users (FL-USERS) access to chemical consultation support from EU-OS medicinal chemistry partners ([CONSULTANTS](#)). The guidelines define: a) FL-USER eligibility criteria; b) CONSULTANT eligibility criteria c) the procedure of CONSULTANT selection; d) the expected feedback from the CONSULTANT to the FL-USER in the form of a FRAGMENT EVOLUTION REPORT. The guidelines do not regulate any confidentiality or IP issues, these should be formalized between the organizations represented by FL-USER and CONSULTANT (e.g. in form of Non-Disclosure Agreement (NDA)), may any of the parties see it necessary.

The interaction of the CONSULTANT with the FL-USER is seen as the first step towards establishing a collaborative chemical biology project (Figure 1) by bringing together the resources, competence, and the capacity to secure funding.

EU-OS fragment library

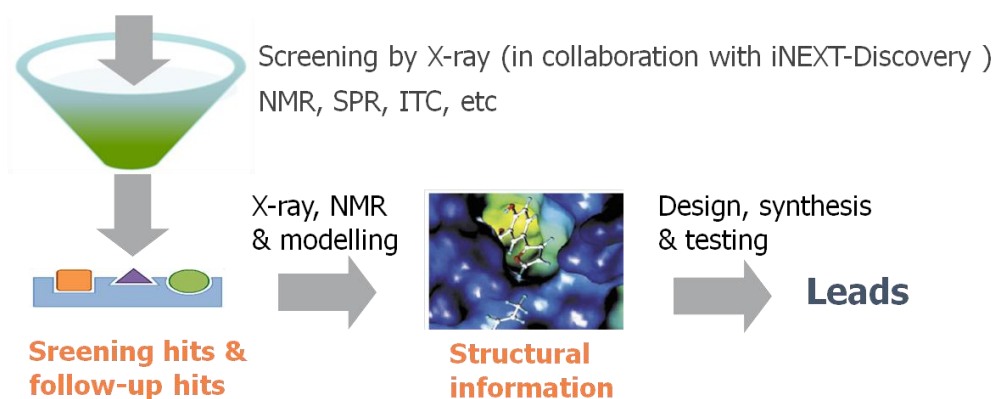


Figure 1. Fragment screening and hit evolution workflow

2 FL-USER

FL-USER is a legal entity (e.g. organization/ research group represented by its legal entity) that uses the EU-OS fragment library to identify small molecule binders for the target of their interest (e.g. protein, RNA, DNA). Within the EU-OPENSSCREEN-DRIVE project, FL-USERS will be at least seven EU-OS and four iNEXT-Discovery (grant agreement No.:871037) partners who have expressed their interest in using the EU-OS fragment library. The form related to the "[Expression of Interest to use the EU-OPENSSCREEN-DRIVE fragment library](#)" (annex 1) is available on the EU-OPENSSCREEN-DRIVE SharePoint for DRIVE members and/ or will be sent *via* email to iNEXT-

Discovery partners upon request. The form needs to be filled in by interested FL-USERS and returned via email at drive@eu-openscreen.eu (indicating “DRIVE-WP4-EoI_partner acronym” within the subject).

3 CONSULTANT

Definition

CONSULTANTS are renowned experts in chemical optimization of fragments to leads/ tool compounds. Each EU-OS medicinal chemistry site nominates one or several CONSULTANTS.

To be registered as a CONSULTANT, he/ she has to provide:

- a) a short description of his/ her expertise;
- b) keywords that facilitate their selection as CONSULTANT;
- c) contact details.

The required information needs to be submitted to the EU-OS central office via email at drive@eu-openscreen.eu (indicating “DRIVE-WP4-consultant registration” within the subject).

Selection of the CONSULTANT

The [list of CONSULTANTS](#) (in alphabetical order) will be available to all FL-USERS through the DRIVE webpage.

The FL-USER should provide a brief description of the project (max 1 page) including:

- a) project background;
- b) current status;
- c) goals;

and identify 3 potential CONSULTANTs by order of priority to EU-OS central office at drive@eu-openscreen.eu (indicating “DRIVE-WP4-consultant selection”) using a dedicated form (annex 2).

The “[consultant selection](#)” form is available on the DRIVE SharePoint (for DRIVE members) and/ or will be made available via email upon request.

If a FL-USER has no preference, the CONSULTANT is selected by the EU-OS central office based on:

- a) specific target disease expertise;
- b) equal distribution of projects among med chem sites;
- c) geographic proximity of FL-USERS and CONSULTANT.

CONSULTANTS are contacted by the EU-OS central office in the order of defined priority. CONSULTANTS should accept/ decline the offer within 20 working days by written notification to the EU-OS central office at drive@eu-openscreen.eu (indicating “DRIVE-WP4-consultant selection” within the subject)

4 FRAGMENT EVOLUTION REPORT

The EU-OS central office notifies the FL-USER about the selected CONSULTANT. The FL-USER requests a FRAGMENT EVOLUTION REPORT directly from the CONSULTANT. The CONSULTANT needs to provide the FRAGMENT EVOLUTION REPORT to the user within 20 working days after receiving the information of the fragment hits from the FL-USER.

The FRAGMENT EVOLUTION REPORT (annex 3) includes the following points:

- a) proposal of follow-ups from EU-OS HTS library;
- b) proposal of commercially available fragment hit analogues;
- c) proposal of synthetic fragment follow-ups based on the synthetic feasibility;



- d) proposal of fragment merging or fragment growth analogues, if structural information is available;
- e) estimation of the work load for the proposed fragment hit analogue synthesis;
- f) proposal of suitable med chem collaboration partner (from EU-OS, iNEXT-Discovery, or external).

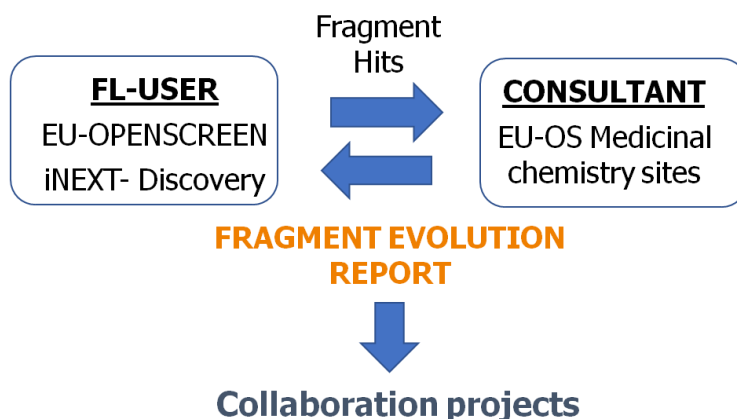


Figure 2 Schematic representation of the collaborative approach envisaged for the development and implementation of fragment screening projects and follow-up steps.

5 COLLABORATION OF USER AND CONSULTANT

After the FRAGMENT EVOLUTION REPORT is delivered, further collaboration of a FL-USER and a CONSULTANT is based on their mutual interest and agreements. Neither the FL-USER nor the CONSULTANT has any commitment on the information delivered, unless regulated by separate mutual agreements (e.g. NDA) between the FL-USER and CONSULTANT. Further collaboration is not in any way restricted or regulated by the EU-OPENSSCREEN-DRIVE project, it can also involve other partners beyond iNEXT-Discovery consortium members and EU-OPENSSCREEN ERIC partners. On the request of the EU-OS central office, FL-USER and the CONSULTANT need to provide information about the progress and outcomes of their collaborative projects.

6 Annex 1 – Expression of Interest to use the EU-OPENSREEN Fragment Library Template

▲ Expression of Interest to use the EU-OPENSREEN-DRIVE fragment library

Date: Click or tap here to enter text.

Partner (including number/acronym): Click or tap here to enter text.

If you are interested in receiving the EU-OPENSREEN-DRIVE fragment library (1000 fragments), please fill in the following sections (approx. length 1 A4 page):

Track record in Fragment Screening (please give a brief overview of past and ongoing fragment screening projects and report relevant publications):

Click or tap here to enter text.

Technologies and equipment that will be used for screening the fragment library (including technologies available for fragment hit validation):

Click or tap here to enter text.

Preferred amount and format (e.g. 25 μ L of 100 mM DMSO-d6 stock solutions; 96 or 384-well plates):

Click or tap here to enter text.

For iNEXT partners only: Please comment on how do you currently organise the med chem support for fragment evolution and your interest in collaborating with EU-OPENSREEN-DRIVE Med Chem sites:

Click or tap here to enter text.

|



This project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 823893

1



7 Annex 2 – Consultant Selection Form Template

Consultant Selection Form within EU-OPENSREEN-DRIVE

Date: Click or tap here to enter text.

Partner (including partner number/ acronym, if applicable¹): Click or tap here to enter text.

This form is intended to be filled in by Fragment Library Users (FL-Users) with the aim to facilitate the selection of a CONSULTANT from the EU-OPENSREEN-DRIVE list of Med Chem Consultants (Names of the Med Chem consultants are listed in alphabetical order at the following link: <https://drive.eu-openscreen.eu/about/medchem-consultants.html>).

Please provide the following information (approx. length 1 A4 page):

<p>Project background (please give a brief overview of fragment screening project background)</p>
<p>Project current status (please give a brief overview of ongoing project activities and follow-up steps):</p>

¹ Partner Number and acronym are available only for EU-OPENSREEN-DRIVE members. For (NEXT) Discovery partners please indicate only institution or affiliation.



This project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 823893



Project goals (please provide a brief description of defined goals for the med chem campaign)

Please propose 3 potential CONSULTANTS by order of priority (1= highest priority; 3= lowest priority):*

1. Click or tap here to enter text.
2. Click or tap here to enter text.
3. Click or tap here to enter text.

*Please notice that if you (FL-USER) have no preference, the CONSULTANT will be selected by the EU-OS central office based on: a) specific target disease expertise; b) equal distribution of projects among med chem sites; c) geographic proximity of FL-USERS and CONSULTANT.

CONSULTANTS will be contacted by EU-OS central office in the order of defined priority. The CONSULTANT should accept/ decline the offer within 20 working days by written notification to the EU-OS central office at drive@eu-openscreen.eu (indicating "DRIVE-WP4-consultant selection")



This project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 823893

2/2



8 Annex 3 – Fragment Evolution Report Template

FRAGMENT EVOLUTION REPORT

Date: Click or tap here to enter text.

Consultant Name: Click or tap here to enter text.

Consultant Institution/ Organization: Click or tap here to enter text.

Please fill in the following fields and return the document to the EU-OS central office at drive@eu-openscreen.eu (including "DRIVE-WP4-Fragment Evolution Report" within the subject) within 20 working days.

<p>Please propose follow-ups from EU-OS HTS library:</p>
<p>Please propose commercially available fragment hit analogues:</p>
<p>Please provide a proposal of synthetic fragment follow-ups based on the synthetic feasibility:</p>
<p>Please provide a proposal of fragment merging or fragment growth analogues, if structural information is available:</p>



This project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 823893

1/2



<p>Please provide an estimation of the work load for the proposed fragment hit analogue synthesis:</p>
<p>Please suggest a suitable med chem collaboration partner for the fragment evolution (from EU-OS, iNEXT-Discovery, or external).</p>
<p>Additional comments:</p>

