opn2EXPERTS - High-concentration liquid formulation of biologics

Using biophysical techniques, how would you propose to enable early-stage screening of biologics for compatibility with high-concentration liquid formulations (HCLFs)?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than January 31, 2024, 11:59 pm PST.

What is the context of the problem that we would like to solve?

The field of biologics is moving towards more patient-centric formulations. The emergence of auto-injectors, pre-filled syringes, and other technologies have substantially reduced patient burden by circumventing lengthy infusion treatments, reducing dosing frequency, and improving convenience. While rapid/self-administration is clearly advantageous for the patient and healthcare ecosystem, enabling this modality presents a significant technical challenge.

Most non-infusion strategies rely on delivering 100-400 mg of drug in a low volume, around 1-3 ml. Thus, one may need a final drug concentration up to 400 mg/ml. Such formulations are known as high-concentration liquid formulations (HCLFs). Currently, about a third of FDA approved antibodies are formulated at or above 100 mg/ml, all of which use traditional excipients, such as polysorbate.

While careful selection of excipients, particularly surfactants, can improve HCLF of some sub-optimal antibodies, others are inherently limited by intrinsic biophysical properties. Protein engineering can be used to modulate the biophysical properties of antibodies but are generally dependent on assays which use substantial amounts of physical materials. Unfortunately, once molecules have reached the scale-up expression stage, it is often too

late to substantially change or re-select molecules and therefore these drugs often pursued as *i.v.* infusions. The ability to screen for HCLF-compatibility prior to scale-up could substantially improve the likelihood of developing a low volume dosing strategy.

To enable earlier screening of biologics for HCLF-compatibility we are looking for low-mass assays which predict HCLF behaviors and enable the profiling of 100's-1,000's of molecules. We would be interested in strategies that could be implemented anywhere from the planning stage (*in silico*) through small scale expression (10 µg-1 mg at ~1mg/ml) using minimal material. What are your strategies to predict the stability, solubility and viscosity of biopharmaceuticals with computational methods or miniaturized low-concentration assays?

What potential solutions could be in scope?

All proposals must include a novel scientific angle or hypothesis and should not simply test an existing technology or method.

- Experimental methods/approaches which aim to miniaturize screening methods that traditionally require large amounts or high concentrations (e.g., rheometer-based viscosity studies). Additionally, proposals seeking to improve existing miniaturized methods will also be considered. Proposals that use standard (commercially available) instrumentation and 96- or 384-well plates are preferred.
- Approaches aimed at evaluating a candidate's compatibility with known HCLF formulation methodologies (e.g., electrospray, nano/microparticle formation, etc.) will also be considered.
- Computational approaches including sequence and/or structure based *in silico* workflows are also within scope but must include a thorough path to experimental validation. All proposals (including AI/ML-based methods) must utilize commercially available software / languages. Methods that are tailored for biologic modalities (instead of proteins in general) will be prioritized.
- Efforts to optimize a novel combination of *in silico* methods, experimental approaches or wet-lab experiments that better predict HCLF-compatibility are also in scope.
- Approaches that identify key biophysical properties of candidates (e.g., viscosity, aggregation propensity, etc.) that influence the molecules HCLF-compatibility.

- Proposals and approaches that are generalizable and extend to non-traditional biologic formats (e.g., beyond IgG) will be favored but are not required.

What potential solutions would be out of scope?

The following will be considered out of scope:

- "Off the shelf" and/or fee-for-service proposals.
- Solutions which require scale-up of material (>2mg) to enable the proposed screening methodology.
- Screening routines that are labor or time intensive. E.g., methods that take >1week or require multiple scientists to complete.
- Proposals that use non-traditional or proprietary buffers.
- Highly complex, or proprietary screening setups (either experimental or computational).
- Strategies that rely solely on modifying the formulations. Furthermore, strategies that include non-traditional formulations or excipients will not be considered.

What benefits do we offer to you in exchange for having submitted a solution?

If your project is selected, you will have the opportunity to directly collaborate with the Protein Engineering Discovery Research team of Boehringer Ingelheim. You can expect appropriate funding for the prospective collaboration period. Your exact funding request should be outlined in your proposal. As a framework, we suggest that your initial funding request is structured in milestone and does not exceed 200,000 euros per submitted project in total.

In addition, depending on the nature of the proposal, we would be open to share an experimental dataset comprised of biophysical measurements (melting temperature, hydrophobicity, and isoelectric point) of at least 100 unique monoclonal antibodies. Furthermore, we would provide sufficient quantities for up to 25 of these molecules to carry out proposed experiments. If your proposal was selected, we would offer experimental/assay support for viscosity measurements, material production, etc. The opportunity for a funded stay at Boehringer Ingelheim for technology exchange / training would also be potentially available.

Our collaboration agreement will provide full transparency about each partner's rights and obligations (including intellectual property rights). As part of the agreement, you will be encouraged to publish following the collaboration agreement (to be negotiated in good faith).

To maintain the highest degree possible in an open innovation environment, we plan to announce the winner(s) publicly and feature them on opnMe.com and our social media channels.

What are the key success criteria on which we base our selection for the best answer?

We would evaluate the research collaboration proposals based on the following criteria:

- A well-structured proposal outlining a new and compelling scientific approach which should not simply test an existing technology or method.
- Outline of the technical feasibility, and potentially existing data or previous publications that support feasibility / experience with outlined technology, based on existing techniques and established assays.
- Proposals that account for traditional formulation conditions will be prioritized.
- All approaches must comply with material limitations (<2 mg).
- Your exact funding request should be outlined in your proposal based on a well-thought-through project. The project should be structured in milestones and planned with key decision points (clear Go/No-Go criteria). The funding request for the initial milestones resulting in a Go/No-Go decision should not exceed 200,000 euros per submitted project in total.
- Proven track record in the required field of expertise.
- Ability to implement the outlined solution as part of a scientific collaboration project with Boehringer Ingelheim including access to a laboratory.

What information should be included in your answer submission?

Please use our answer submission template to provide a 2–3-page non-confidential proposal (available for download on the following site).

If confidential data exists that would strengthen the proposal, please indicate that information is available to share under a Confidential Disclosure Agreement (CDA). If we find the non-confidential concept proposal sufficiently interesting, we will execute a CDA for confidential discussions.

Anticipated Project Phases or Project Plan

Phase 1	Please complete your submission by **January 31, 2024, 11:59 pm PST** at the very latest
Phase 2	Our review of all proposals will be completed through mid-March 2024 and submitting experts will be informed after that.
Phase 3	Potential collaboration starting date in Q3/2024

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "High-concentration liquid formulation of biologics" question on opnMe.
- Alternatively, you may click the "Get Submission Template" banner to access the material transfer template.
- Follow the instructions to upload your submission document (requires login or registration).
- The upload allows you to attach additional application files if desired.
- You will be able to access your final submitted collaboration proposal in your personal dashboard and follow its review status.
- Please also visit the FAQ section on opnMe.com to learn more about our opn2EXPERTS program.

References

1. Zarzar J., Khan T., Bhagawati M., Weiche B., Sydow-Andersen J., Alavattam S. High concentration formulation developability approaches and considerations *MAbs*. **2023**, 15(1):2211185. DOI: 10.1080/19420862.2023.2211185, PubMed.

2. Wang S. S., Yan Y. S., Ho K. US FDA-approved therapeutic antibodies with high-concentration formulation: summaries and perspectives *Antib Ther*. **2021**, 4(4):262-272. DOI: 10.1093/abt/tbab027, PubMed.