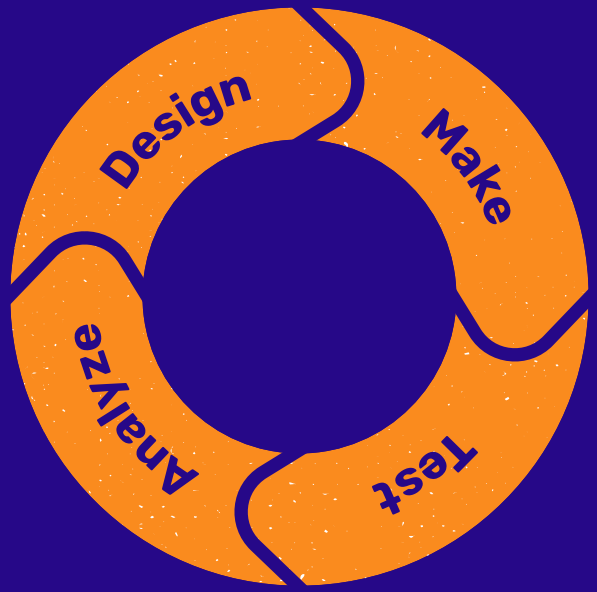
Chemaxon



Project management in the DMTA cycle

Prioritizing and keeping track of design, synthesis, and test results in a collaborative fashion

Challenges when prioritizing and keeping track

When optimizing drugs in the DMTA cycle, there are two main challenges:

1

The science

What should the drug compounds look like, to safely cure the disease?
What are the current issues/questions and parameters that need to be improved, how to interpret experimental results, and how to design optimized drug compounds?

2

The resources

How to allocate the FTEs, how to distribute the budget, and which assays to run for which compounds

The DMTA project leader's two main tasks are to simultaneously optimize the molecules and to prioritize all ongoing team activities. The priorities depend on which resources are at hand, as well as the results from experiments: which are the most promising compounds right now? Do we have a candidate drug in our hands – or what modifications should be made next, to optimize the compounds to clinical candidate quality?

The many uncertainties in drug discovery are not only related to optimizing the efficacy and safety of a drug in different in vitro or in vivo systems, but also in estimating the time to synthesize a novel compound, or knowing when a required starting material will arrive from your CRO.

Design Hub enables efficient compound design, synthesis, and progression tracking via an interactive Kanban board, ensuring the success of drug development projects.

Kanban in Drug Discovery

Optimizing drug discovery and team efficiency

Interactive Kanban board for drug discovery

A multi-dimensional, chemically searchable, and interactive Kanban board can help the project team get a comprehensive visual overview of the ongoing activities. This facilitates distribution and prioritization of work.

The Kanban board in Design Hub has three levels, facilitating the overview of ongoing hypothesis, design sets, and individual compounds being synthesized. The board can also be connected to databases with available starting materials and to an electronic lab notebook (ELN), with further information needed to estimate the time to finalize a synthetic procedure. Visualizing this information via the Kanban board facilitates decision making.

Kanban is Japanese for 'billboard' or 'signboard' and was first used in the 1950's by car manufacturer Toyota, aiming to improve the efficiency and quality of production.

By visualizing both results and rate-limiting factors of the overall process, resources can be shifted from less crucial or problematic tasks to activities with higher impact.

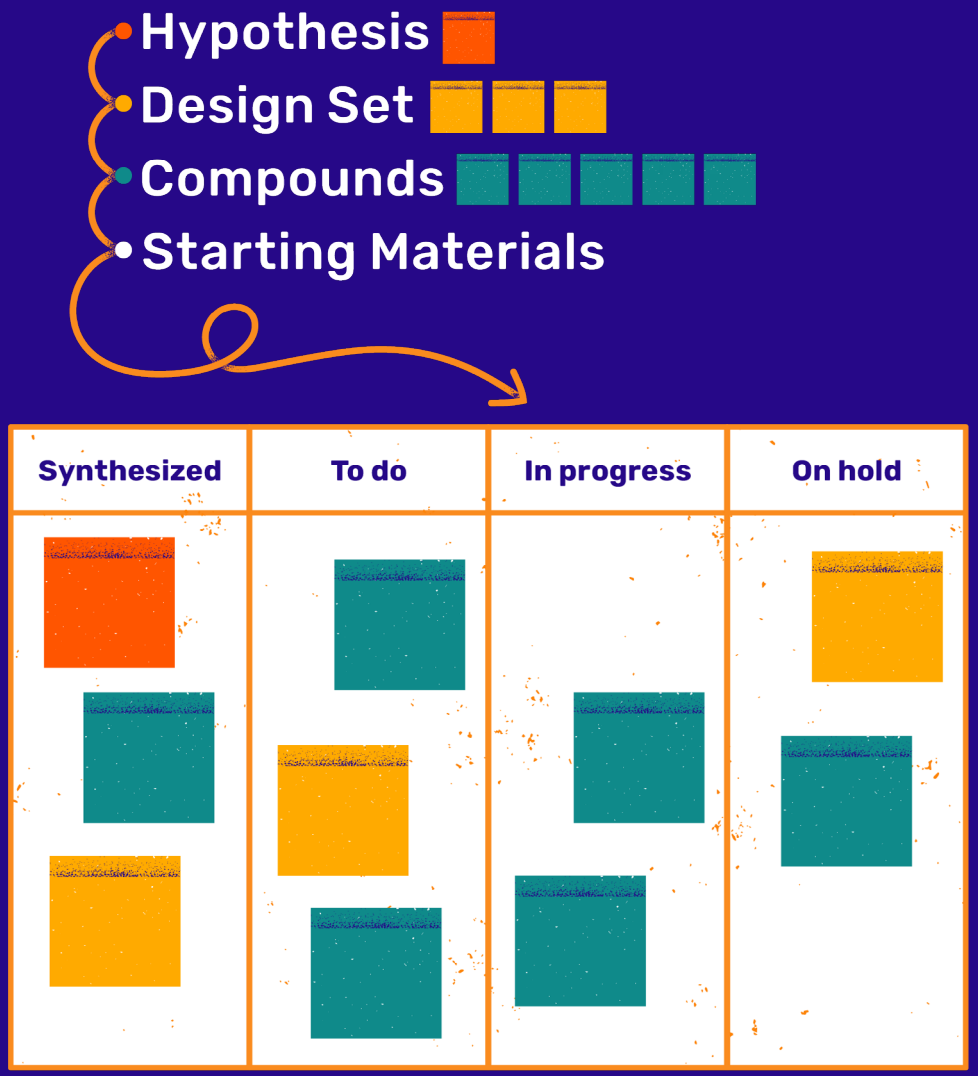
The transparency of the Kanban board also enhances the employees' sense of shared responsibility and enables understanding of issues, thus facilitating innovation.

An interactive Kanban board allows teams to keep track of who is performing which tasks on several levels (Hypotheses, Design Sets, and Compounds). Each level can be viewed on a two-dimensional, dynamic board showing assignee, status, priority, or tags on any of the axes. Each level is searchable and can be filtered on both text and chemistry. Time spent on each task is automatically measured. Cost and value for each task can be annotated.

Capabilities of the Design Hub Kanban board

Show, sort, filter, search for…

- Project member
- Assignee
- Chemical structure
- Status
- Priority
- Tags
- Time spent per task
- Hypothesis, Design Set, and Compound hierarchy



What is Design Hub?

Design Hub is a drug design software that connects scientific rationale, project data, and computational resources. The application takes data-driven drug design to a whole new level while keeping your costs low.

Design Hub is an integrated lead optimization application by Chemaxon for medicinal chemistry teams. Built on the best-in class chemical drawing capabilities of Marvin JS and structure storage options of JChem Microservices, the application connects scientific rationale with compound tracking and computational resources needed for guided chemical structure design.

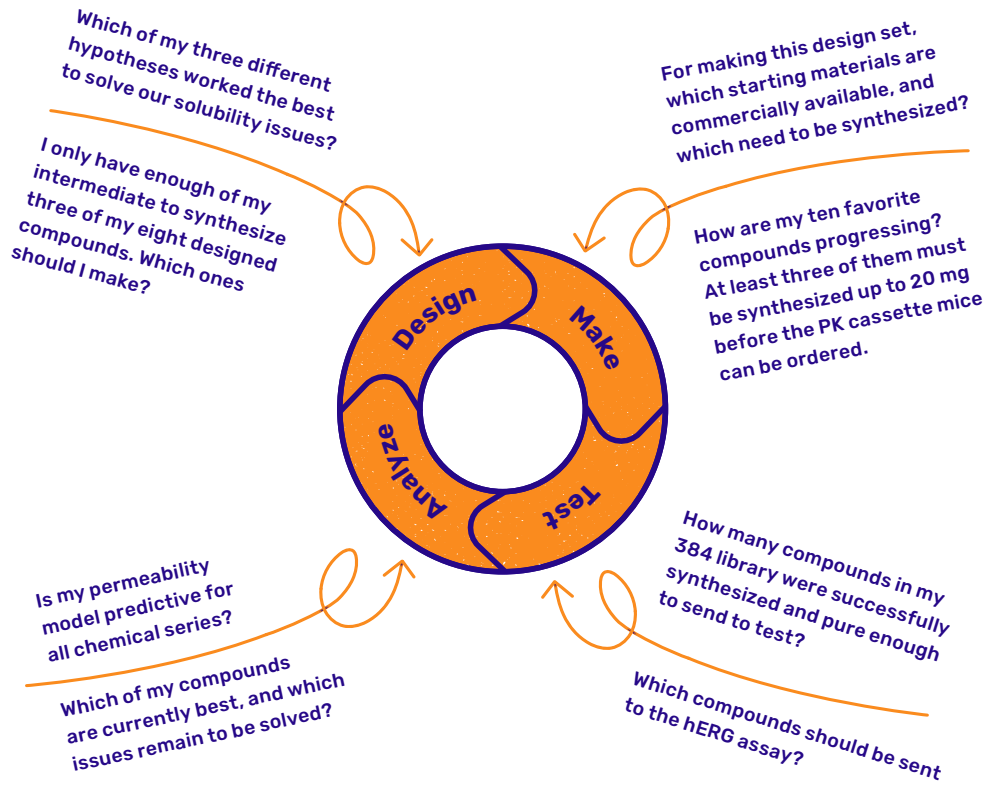
This structured data then enables productivity boosts such as team Kanban boards, automatic status updates for compounds, and a universal query capability that combines chemical, text, and metadata options.

Design Hub

Examples of DMTA decisions

In a drug discovery project, vastly more potential compounds can be imagined than can be possibly made. A project leader's constant question is how to prioritize the paths which should get resources spent towards the clinical candidate.

The Design Hub platform presents all information needed, and with the Kanban board facilitates not only decision making but also allocating FTEs and priorities to new tasks.



Kanban connected to... DESIGN

Which of my three different **hypotheses** worked the best to solve our solubility issues?

It seems like we are still lacking data to make a conclusion on this last hypothesis for solubility. We should delay making new designs to test these hypotheses until next week, when all data should be in place for a thorough analysis

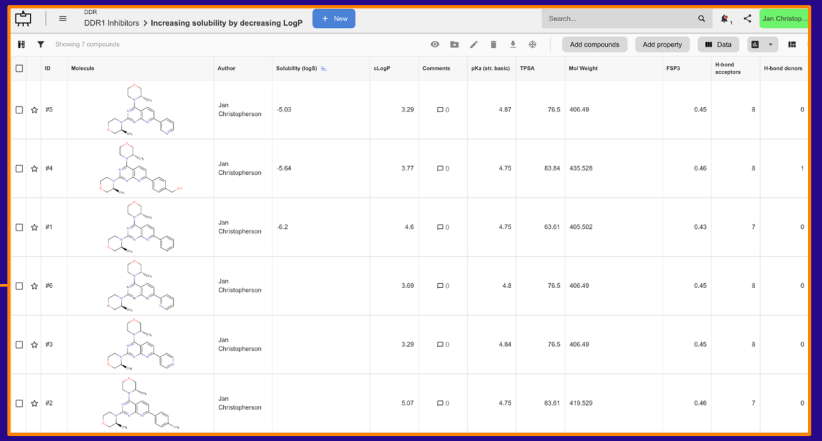


Figure 1.
The Kanban board has direct connections from the planned compounds to their corresponding hypothesis, predictions, and data.

I only have enough of my intermediate to synthesize three of my eight designed compounds. Which ones should make?

Comparing predicted properties of my eight designed compounds tells me that these three are my best candidates. The Kanban board shows that our "JC CRO" seems to have only a few compounds left "In synthesis". OK, I'll assign these to them.

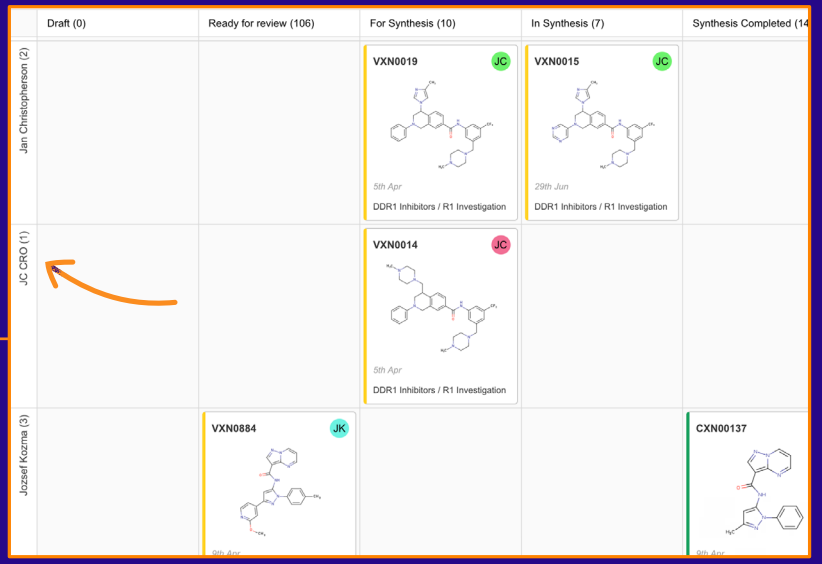


Figure 2.
The assignees can be individuals – or even another company, such as a CRO, who (optionally) will see only those compounds assigned to them.

The titles and number of columns of the Kanban board can be customized according to user preferences.

Kanban connected to... MAKE

To make this design set, which starting materials are commercially available, and which need to be synthesized?

Only two out of six starting materials are commercially available. I need to allocate someone to synthesize the missing ones.

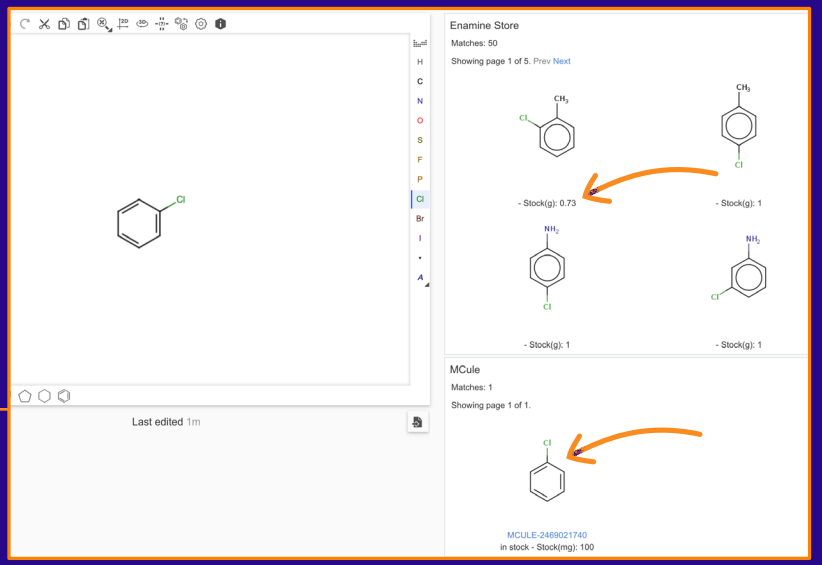


Figure 3.
Information on the number of steps to synthesize a compound, starting material availability, and cost can be stored at the compound level.

Starting material availability can be displayed via connections to external databases.

How are my ten favorite compounds progressing? At least three of them must be synthesized up to 20 mg before the PK mice can be ordered.

Looking in the ELN, it seems like the most important compound is stuck in synthesis on the third step. I will suggest an alternative synthetic route!

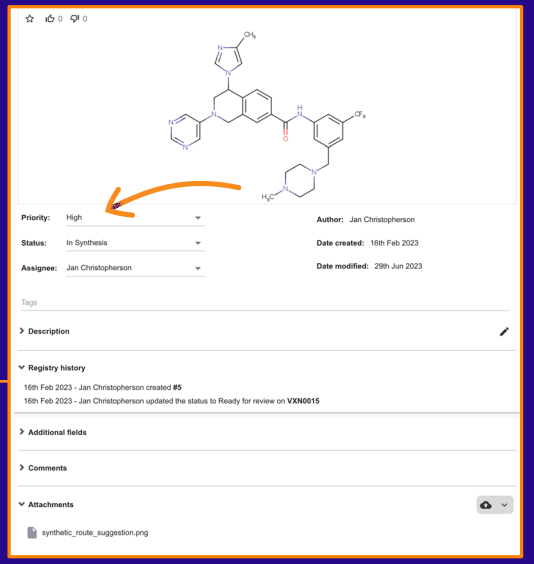


Figure 4.
From the Kanban board, links and file attachments connected to Hypothesis, Design sets, and Compounds an be easily stored and found

Kanban connected to... TEST

How many compounds in my 384 library were successfully synthesized and pure enough to send to test?

The library synthesis went really well! Only two compounds failed, which were not particularly important. I consider this library DONE and the compounds can be sent to test.

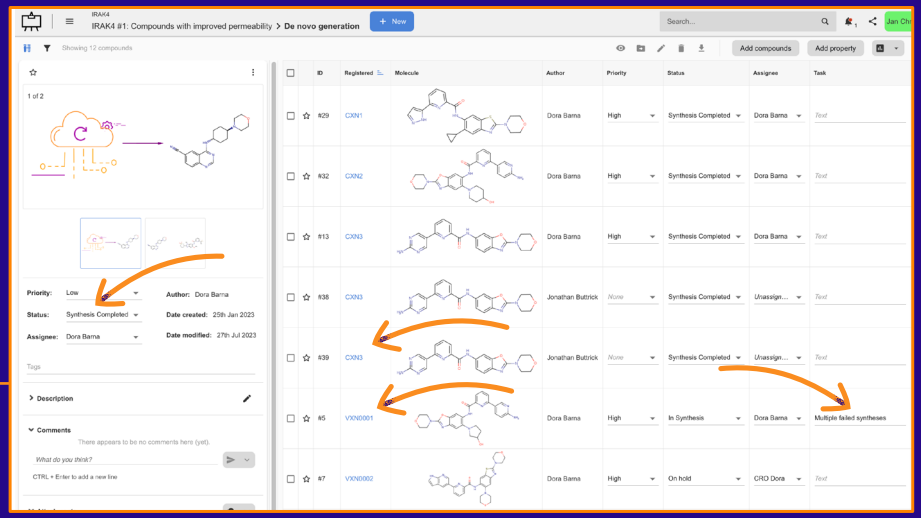


Figure 5.
Design Hub can be connected to your internal compound registration database, so the virtual IDs get automatically updated to internal IDs upon registration of the synthesized sample.

Which compounds should be sent to the hERG assay?

From the comment, it seems like this compound is not pure enough to send to hERG assay. I'll assign it for resynthesis.

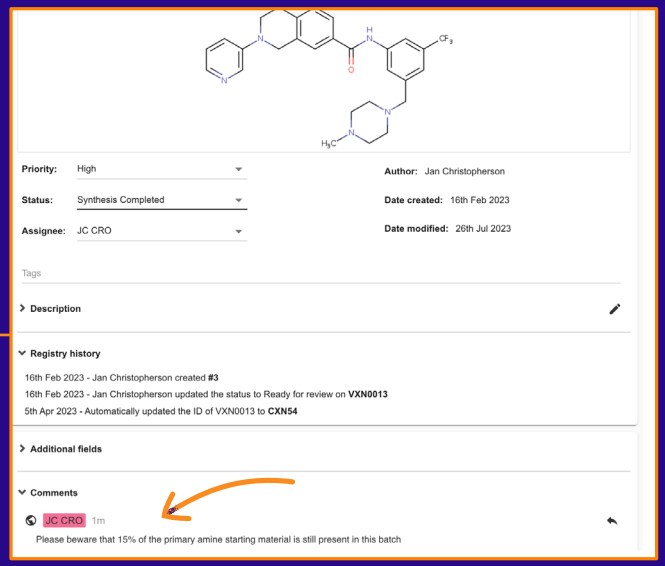


Figure 6.
Comments are available for everyone, facilitating discussion and collaboration.

Is my permeability model predictive for all chemical series?

The new data suggests that the permeability model is no longer predictive for compounds with a hydroxy group in series A. I'll assign all such design-sets to our computational chemist to look at, prior to selecting additional compounds for synthesis…

> Learn about how local and global models are used in predicting properties of small molecules

Which compounds are currently my best ones, and which issues remain to be solved?

Wow! The recent data shows several compounds fulfil our desired potency and bioavailability profile. I will send them all to the safety panel immediately – at least one of them should be good enough for efficacy studies? And since this type of compound has been quite time-consuming to make, I'll ask for the common intermediate to be scaled up now, to address the tight deadline.

Kanban connected to... ANALYSIS

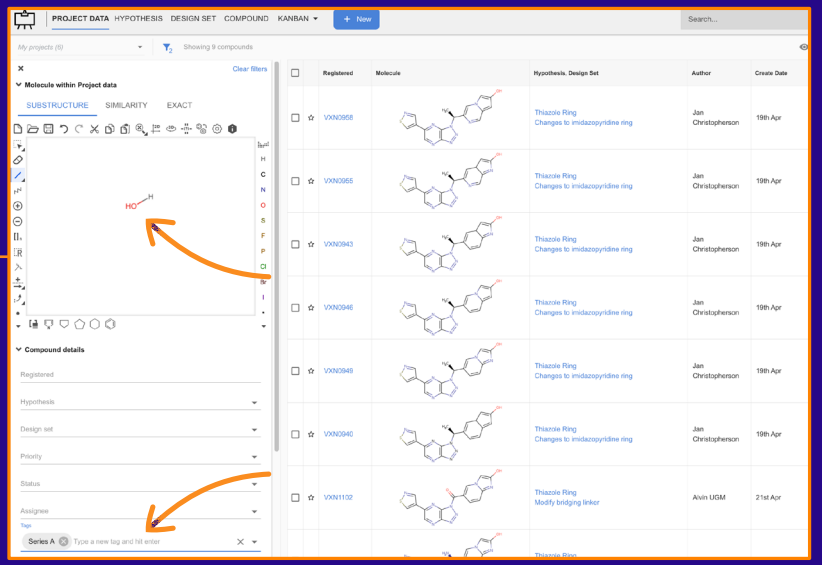


Figure 7.
The Kanban board can be searched and filtered by structure or text, showing only content of interest.

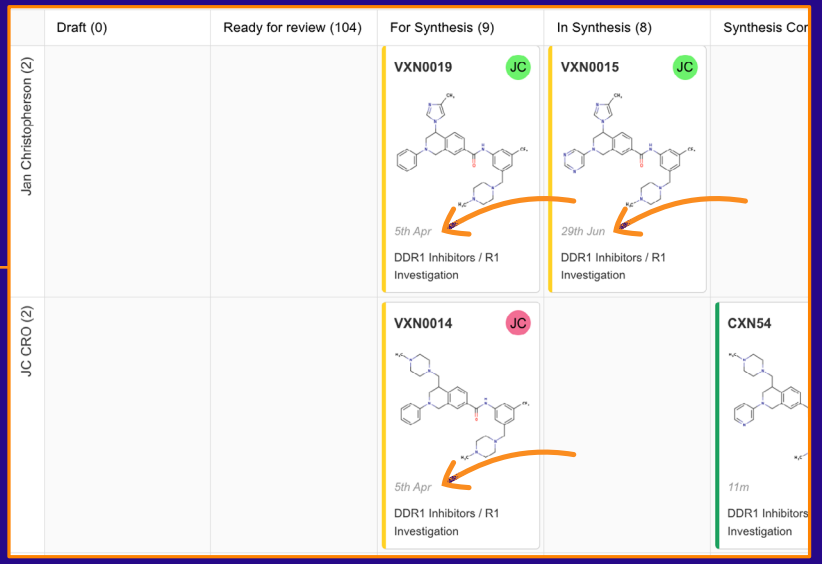


Figure 8.
The time spent to finalize each task (for instance compound synthesis) is automatically counted, from the start of the task.

Collaborate on original research with your medicinal and computation chemist peers. You can track compounds, identify and optimize leads while working with remote teams. Browse legacy projects and build on your internal knowledge base instantly.

Chemaxon offers single tenant setups, which are available using AWS infrastructure. The company and all its vendors are ISO certified, offering further peace of mind regarding secure handling of your data.

We provide a highly available system with frequent updates, built on a cloud infrastructure so you are not limited as to the capacity you need access to in an instant. The system has role- and project-based access, with the granularity necessary for sharing information with CROs, while keeping your IP safe.

Learn more about how Design Hub makes collaboration with CROs smooth.

Conclusion

There are two key factors to handle when optimizing drugs in the DMTA cycle. The scientific part, dealing with research questions and results, is usually considered the more important. However, for efficient project execution, it is equally important to prioritize the tasks and resources well, such as budget, FTEs, and assay capabilities. With its innovative features and capabilities, such as the Kanban board for keeping track of progress of any of the hypothesis/design set/compound and starting material levels, Chemaxon's Design Hub is engineered to make project progress as well as collaboration and information sharing within a drug discovery project smooth and secure. It streamlines project management, makes it easy to communicate and share data, and gets you to designing and synthesizing compounds quickly while ensuring data security and protecting intellectual property.

For more info contact us

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