

FAQs

What is KerusCloud?

KerusCloud is a uniquely powerful and innovative study simulation software platform that ensures clinical studies are suitably designed statistically from the outset to maximise their chances of success. To do this, KerusCloud creates highly realistic synthetic data sets (virtual populations) which provide the basis for generating thousands of study simulations that accurately mimic the complexity of real clinical studies. This allows researchers to examine the performance of a wide variety of study design and analysis options in silico, in minutes and choose the best options for real studies going forward.

Why has KerusCloud been developed?

KerusCloud has been designed by statisticians at Exploristics with many years experience of clinical development in the Pharmaceutical industry to address the problem that current study design tools do not adequately support the designs of modern clinical trials that are generating increasingly complex clinical, demographic and biological data.

New approaches, such as Precision Medicine, have led to clinical trials that need to answer multiple questions such as understanding the association of risk factors on treatment response and identifying subgroups of patients that derive benefits of treatment. However, the majority of design tools assume that only one factor influences variability in treatment response (eg. Treatment) and it is common practice to make simplistic, fixed assumptions about the nature of the relationship between that factor and response. This traditional approach to designing studies is statistically crude and fundamentally flawed as it does not adequately account for the multiple sources of uncertainty in real studies nor does it make best use of available data and the skills of the statistician who are often brought into the design approach at a late stage of clinical protocol development.

Consequently, Exploristics has built KerusCloud, a software platform that can handle the many sources of uncertainty that should now be considered when designing a clinical study. This powerful and versatile simulation platform gives statisticians an invaluable statistical tool with which to engage much earlier in clinical protocol development and de-risk clinical trials from the outset. KerusCloud does this by offering a more efficient data-driven approach to study design that can account for the complexity of modern clinical trials and ensure that fewer studies will fail for avoidable statistical reasons. With KerusCloud in their toolbox, statisticians can play a central role in improving study design at every phase of clinical development, driving down historically high attrition rates to accelerate the rate at which new medicines, diagnostics and devices reach those with unmet clinical need and improve the return on R&D investment in the process.

How is KerusCloud different from other commercially available software?

KerusCloud is the only statistical software available that can evaluate multiple aspects of clinical trial design simultaneously. It is also the only cloud-based simulation tool that harnesses the power of cloud computing to speed up simulation. This means that using KerusCloud ensures that the best combination of study design and analysis options can be assessed and selected for real studies in minutes, so that they can achieve statistically and clinically meaningful outcomes. No other commercial software can process and simulate the complexity of multiple correlated study variables and outcomes as KerusCloud does. Other software can simulate data and perform tests, but this is generally limited to either simulation of single variables or multiple independent variables which only crudely reflect real clinical studies. This unique ability to process multiple correlated variables and outcomes as well as subgroups and missing data means that studies simulated with KerusCloud are exceptionally realistic and informative as they closely mimic the complexity of biological, clinical and real-world data.

Why are these unique capabilities useful?

KerusCloud is uniquely useful as it is the only software platform that can generate virtual patient populations that are the most realistic representation of data collected in modern clinical research. It can model variables based on any of the most common data types and statistical distributions, as well as the correlation between variables. This innovation is the result of many years of research and development on copulas for generating complex multivariate data that ensure the properties of the marginal distributions as well as the correlation structure is maintained.

Consequently, KerusCloud can generate complex data comprising:

- Common features such as subgroups and strata, risk factors/covariates, multiple outcomes
- Special features including derived variables, missing data, truncation and censoring

Using this highly realistic virtual data and its intensive processing power, KerusCloud can run thousands of Monte Carlo simulations in minutes to evaluate the probability of success of many, varied study designs and analysis options to achieve study or programme objectives. KerusCloud has increased processing power with up to 96 parallel cores for a single simulation and an intelligent process management system which boosts processing power as needed, so even the most complex simulations can be run in minutes and the results reviewed in real time. KerusCloud is hosted on Amazon Web Services (AWS), where the Kerus statistics engine benefits from the scalability and performance of the cloud. This allows KerusCloud to produce results in minutes, even for large and computationally intensive simulations.

How else is KerusCloud uniquely useful?

With clear state of the art graphical displays and streamlined workflows, KerusCloud facilitates earlier engagement between statisticians and clinical R&D teams in the study design process, allowing the impact of different design and analysis choices to be simply visualised, compared and interpreted by the whole team in the process of study optimisation. In this way, KerusCloud enables all researchers to bring statistical considerations into the foundation of any development project so that clinical studies are fully optimised in silico to increase real study success rates.

Where does the data come from for generating virtual study populations?

KerusCloud offers unparalleled realism with the virtual populations it generates. The real data used to create these synthetic data sets comes from multiple sources, including the scientific literature, patient-level data and expert opinion. Patient-level data can be automatically imported into the platform via our innovative Kerus Data importer (KDi) technology in the form of summary statistics from existing patient-level data sets. Many users of KerusCloud have access to their own internal patient databases. Alternatively, Exploristics sources its patient-level data from a range of databases and exclusive partnerships developed between our Data Strategy Team and data providers.

A common source of patient-level data comes from investigator-led observational studies. These studies are instrumental as they typically contain the risk factors and endpoints, measured over timeframes, that are relevant for clinical trials. Such data is further augmented by publicly available statistics from the published literature and insights from experts and key opinion leaders (KOLs) in the relevant therapeutic field. All data sources are synthesised into an integrated database that captures the relevant knowledge and associated uncertainty using a range of data models.

What skill level is required to use KerusCloud?

KerusCloud has been designed to be used by statisticians involved in the design of clinical trials to facilitate evidence-based decision-making by all stakeholders in clinical development through study simulation. However, as KerusCloud does not require programming skills it is easy to master with appropriate support and a working knowledge of variable distributions and correlations. This is facilitated by the software's intuitive point-and click user-interface which makes it easy to set up a project and navigate through the input and analysis of data.

Who is the typical end user of KerusCloud?

Typically, end-users are statisticians seeking to bring a quantitative approach to early decision-making when clinical research teams are selecting the design and analysis approach to be taken for a study. KerusCloud gives statisticians the means to provide a robust statistical basis for any study design, removing personal bias by ensuring that design and analysis choices are made empirically from the outset. By providing a quantitative framework for early decision-making when many study parameters may be unknown, KerusCloud enables statisticians to demonstrate to the broader clinical teams both numerically and visually which design choices are most likely to deliver meaningful answers to complex clinical questions. This method dramatically improves the probability of success of real-time studies, de-risking study protocols and shortening development timelines.

How secure are my data, simulations and results within KerusCloud?

KerusCloud offers best in class security with unparalleled cloud security measures and multi-factor authentication for complete control over access rights. KerusCloud is deployed in a "Virtual Private Cloud" on Amazon Web Services (AWS) which is logically isolated from all other virtual networks and harnesses the security already provided by AWS. Here, KerusCloud data is protected by multiple layers of security so that only the owner of what is stored can gain access. KerusCloud does not store any real patient-level data; only summary statistics from real data are stored, and these are used to generate synthetic data (virtual patient populations). Finally, Exploristics works

with third party cybersecurity experts for the purpose of penetration testing to ensure that our platform remains secure against cyber attacks.

What type of organisations benefit from using KerusCloud?

KerusCloud is a unique software tool principally aimed at healthcare organisations seeking to accelerate the development of new medicines, diagnostics and medical devices by improving clinical study success, and so return on R&D investment. These include companies involved in the development of pharmaceuticals, biotechnology, medical technology, clinical diagnostics as well as academic research institutions and contract research organisations (CROs). However, KerusCloud is also a versatile and useful tool for organisations outside healthcare interested in generating and analysing synthetic data more generally in order to protect data privacy and confidentiality.

What size of organisation benefits from using KerusCloud?

KerusCloud is a useful statistical tool for organisations of any size. For smaller organisations without in-house statistics teams, it can be accessed via our statistical consultancy services which provide full wrap-around support. For larger organisations, KerusCloud can be accessed via a licence by in-house statistics teams and used either alone or alongside other statistical software to support earlier statistical intervention or augment the design of research studies in emerging research areas such as precision medicine, and real-world data approaches. KerusCloud is also available via a licence to CROs and independent networks of freelance statisticians who provide statistical services to their own customer base. Exploristics is able to offer training to support this.

What is the KerusCloud pricing strategy?

Exploristics' pricing and licensing strategy aims to avoid inflexible pricing models of other software packages where customers pay a significant fixed amount whether they use the software or not. KerusCloud pricing and licensing is based on a software as a service subscription model. The price is comprised of two components: a user fee which is a fixed cost to provide ongoing access to the platform, accounts, training and support; a usage fee which is a flexible cost that relates to the amount of use.

We use a system called Kerus Credits to manage the usage costs. These are tokens that can be purchased in blocks which decrease in cost with increasing block size. Kerus Credits are very flexible as they can be shared with users within the same organisation, carried over and spent on other things such as setting up new users, or for additional training or support.

We monitor the availability and the use of credits. This allows us to create flexible, bespoke licensing agreements that scale in a cost-effective way by bundling the the user and usage components into a single subscription. This way, the licensing agreement is completely aligned with the needs of the customer.

How quickly can KerusCloud be implemented?

On purchase of a licence and accessed via our statistical consultancy KerusCloud can be implemented straight away. Accessed via a licence for in-house or individual use, how quickly KerusCloud can be used is dependent on the statistics experience of the user. For users with in-depth statistics experience, its simple workflows and intuitive interface allow users to navigate the point-and-click system to build, evaluate and manage large numbers of study scenarios in minutes. To facilitate this, we provide a user guide, tutorials, case studies and wrap-around support so that you can get your project up and running as quickly as possible. With some initial training and guidance, KerusCloud is also accessible for those with moderate statistics experience as its clear workflows lead users through the processes for creating virtual study populations, inputting study assumptions, specifying the variables for evaluation, defining

success criteria, and running study simulations. For all, the results are easy to visualise and explore via an interactive heatmap, ensuring effective communication within and across research teams and areas of expertise for more inclusive and effective decision-making.

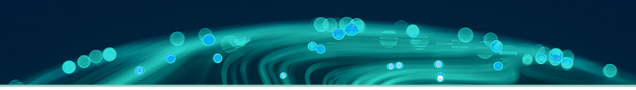
When can KerusCloud be used in the clinical development process?

KerusCloud is an invaluable tool throughout clinical development and can be used to optimise the design and analysis approaches of Phase 0-4 studies. Used from the outset of the development process, KerusCloud ensures that key development decisions are fully data-driven and that all studies are comprehensively optimised to ensure that meaningful insights can be drawn from them. This gives development programmes a strong statistical basis to build from at each phase, improving the efficiency with which investigational products progress towards approval. The virtual patient populations generated by KerusCloud can also be used to explore a range of scenarios at an interim analysis and guide optimal ways to proceed depending on those interim results, particularly for adaptive designs.

Are there stages of clinical development where KerusCloud adds particular value?

While useful at any phase, KerusCloud adds considerable value in creating a robust evidence package in Phase 2, where achieving proof of concept can unlock the potential for out-licencing or further investment. Phase 2 studies are often a crucial stage in determining initial proof of efficacy but currently are frequently not an effective predictor of success with over 30% of drugs entering Phase 2 studies failing to reach Phase 3 and a further 58% of drugs that do progress at this stage going on to fail in Phase 3 (reference). More effective design and analysis of Phase 2 studies ensures that pivotal studies at Phase 3 have a greater chance of success.

Whilst the transition from early to late-stage clinical development is a critical juncture where KerusCloud adds significant value, the software has broad utility in other studies. KerusCloud provides invaluable support for de-risking expensive late-stage studies and ensuring that



they are able to generate evidence to support labelling claims. It can also support complex innovative designs such as multi-stage studies, seamless designs, adaptive designs and pragmatic studies.

How can KerusCloud improve R&D productivity?

KerusCloud offers many unique capabilities and so can improve productivity in several ways whether deployed alone or in conjunction with other commercially available statistical software.

Firstly, it improves the productivity of R&D teams by ensuring that development is derisked efficiently by fully optimising design and analysis approaches in silico prior to embarking on real studies. Close consideration of the numerous factors that can impact a study at this early stage, ensures that real studies are less likely to fail for avoidable reasons and can achieve statistically and clinically meaningful outcomes. Driving a rigorous evidence-based approach, KerusCloud ensures that key operational characteristics of studies such as target population and study duration are effectively optimised. By providing reliable estimates for optimum trial/study requirements such as sample size, KerusCloud ensures that studies recruit/process the minimum number of patients/samples to achieve adequate statistical power, minimising wasted processing time, reducing sample wastage and decreasing risk to patients while ensuring a substantial likelihood of success.

Secondly, KerusCloud ensures that statisticians can be more productive and influential in the development process as it enables them to improve and refine trial design faster and more efficiently than by writing and validating their own code, typically reducing an activity that may take weeks or months into one that can be complete in hours or days.

How can KerusCloud help inform decision-making?

KerusCloud helps researchers to pinpoint which key study parameters will be most influential in achieving study success. With a user-defined threshold for an acceptable

probability of success, KerusCloud supports R&D teams in making informed decisions about trial or experimental designs by simultaneously examining many variants of trial or experimental configurations, providing a simple interpretable summary output including a intuitive heatmap to identify risks or factors to enhance the costeffectiveness or time-efficiency of the study.

How has the KerusCloud approach helped previous users design their studies?

The KerusCloud approach has been instrumental in helping organisations improve success rates with optimised study design and analysis options to de-risk and accelerate development. This has included identifying the best study endpoints, study participant number and target populations to increase success, saving time and costs as well as developing robust evidence packages to support investment or regulatory engagement, increasing the value of development pipelines.

Multiple case studies using the KerusCloud approach are available on our website at exploristics.com/casestudies/.

Could KerusCloud be used as part of any engagement with regulatory authorities?

Yes, the output from KerusCloud has been validated versus established statistical software and has supported submissions and engagements with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). It has been developed with reference to applicable FDA and EMA guidance and published industry standards for good simulation practice. It has also been used in a case study to support the EU's Medicines Adaptive Pathways for Patients (MAPPs) initiative which is looking at ways to enable early access to novel treatments for patients with severe unmet need.

What if KerusCloud doesn't currently do what I need?

The development of KerusCloud to date has focussed on the ability to generate realistic synthetic data, the exploitation of processing power in the cloud, the point-and-click interface and user experience, the interactive graphics and the intuitive workflow. Currently, KerusCloud offers the study design and analysis capabilities provided by other study design tools as well as its own unique functionality. KerusCloud is extremely easy to use and can solve, entirely or in part, most simulation problems. Nevertheless, we are constantly updating the software based on customer feedback and have an ambitious development roadmap where the next stage of development will focus on building out the data, design, analysis and decision capabilities.

Meanwhile, to address more complex design problems we allow access to the simulated, multivariate data to enable the use of other tools for functionality that does not currently exist within KerusCloud.

At Exploristics we value engagement with all our customers and listen to what they say they need. Consequently, users of KerusCloud are encouraged to input into the roadmap so that we can prioritise the functionality that is in development. As the software has been built in an adaptable and scalable way, we are able to continually add new functionality. We work on a three month development cycle and new functionality is made available to beta-users immediately on release.

Choose KerusCloud
Delivering quantitative decision-making support for your study design and analysis approaches.

