# *In Vivo* Research Management

## Climb™ Lab 360° Collaboration Suite



*Digitalizing In Vivo Research*

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# Introduction

## Climb™ 2.0: A Lab Informatics Platform for Pharmaceutical and Biotech Companies, Contract Research Organizations, and Academic Research Laboratories.

Biomedical research is process and data intensive, requiring multidisciplinary collaboration between individuals, across geographical locations, and with external organizations. This broad collection of people, skills, departments, sites, and contractors working together on highly regulated, technical, and expensive research creates an enormous challenge to effective management.

According to RockStep Solutions surveys, over 70% of pre-clinical research and development (R&D) organizations continue to rely on paper, spreadsheets, share folders, or homespun solutions, creating data silos and fragmented analytical environments. In these environments, data are difficult to locate and compile for analysis, QC checks, and regulatory reporting, particularly for research programs operating at scale or working towards an investigational new drug (IND) submission. Wasted staff resources and time delays in getting from discovery to IND submission can be costly to an industry already struggling with procuring acceptable return on investment (ROI) from R&D expenditures. A recent investigation found that from 2009-2018, the estimated mean investment into research and development to bring a new drug to market, accounting for failed trials, was $1.3B[1].

New cloud-based Laboratory Information Management Systems (LIMS) are emerging that address some of the challenges of managing data, workflows, animal colonies, and samples; however, most are point solutions that solve specific problems and do not address the critical issue of fractured data silos.

Climb™ 2.0, from RockStep Solutions, is an enterprise solution that addresses the entire spectrum of challenges in one integrated package. Operations and data management needs are solved within one seamless software application. Architected in the cloud and delivered as software as a service (SaaS), Climb can be used by small labs or enterprises to manage biomedical research operations and data. In addition, Climb is highly configurable and can integrate with other technology tools, enabling this solution to support any research stream.

This white paper presents sectors in biomedical research where Climb is used to address research challenges and highlights some of the Climb use-cases. For more information about Climb, please visit https://www.rockstepsolutions.com/ or email us at info@rockstepsolutions.com.

# Eliminating Data Chaos

The ROI for R&D in the biomedical industry is showing signs of breaking the downward trend, due in part to improvements in collaboration, efficiency, and the digitalization of drug discovery[2]. Data scientists spend an average of 45% of their time wrangling data rather than doing the analysis that brings value to research[3]. As efforts to develop new drugs and therapies rely more and more on "big data", the data corral is getting crowded. It is not unusual to find a single share folder with thousands of spreadsheets of study data. Highly skilled data wranglers are now needed to locate, QC, merge, aggregate, and harmonize data for analysis.  These manual processes are not only costly, they are also error-prone and can lead to missed discovery opportunities or false starts at a time when efficiency and quality improvements are essential.

## Challenges for bioinformatics and data analytics

- Locating data
- Conducting data QC
- Harmonizing data
- Searching and combining related data across time and studies
- Developing a 360° view of experiments, research animals, and associated data
- Managing secure data access and delivery to research collaborators
- Preventing data loss or destruction

## *Use Case – Aggregating and Harmonizing Data at Jackson Laboratory*

In a recent Climb deployment at Dr. Gary Churchill's laboratory in The Jackson Laboratory, RockStep loaded 1,300 legacy spreadsheets and media files with over 93,000 data points collected for an industry collaborative aging study into Climb.  As part of this deployment, RockStep created data import templates so future study data could be easily imported directly from instrument outputs into Climb via a drag-and-drop interface. For this research program, Climb enabled multisource data to be queried and exported in standard formats.  Data wranglers no longer had to spend hours and days cutting and pasting data for quality control (QC) checks and organizing data for analysis.

> **"… the time we'll save retrieving, quality checking, and analyzing data will significantly increase as the studies progress and we accumulate data,"**
>
> **- Gary Churchill, Ph.D.**
>    Professor Karl Gunnar Johansson Chair, The Jackson Laboratory

# *In Vivo* Workflows for Drug Discovery

High-throughput *in vivo* drug discovery workflows place intense demands on lab technicians and animal caretakers who must move quickly through their tasks of locating animals, taking measurements, injecting compounds, or conducting physical exams. In addition to challenges in the animal rooms, lab managers must be able to schedule tasks, manage resources, and have full situational awareness of progress and daily operations. Finally, scientists need to aggregate data from multiple sources across studies, departments, and occasionally external organizations, to draw accurate conclusions from collected data and delineate the appropriate next steps in the research process.

## Challenges for *in vivo* drug discovery workflows

- Managing and scheduling resources
- Locating the correct animals for testing
- Logging activities and recording data
- Communicating between vet staff, lab managers, scientists, and technicians
- Quality checking data
- Aggregating data for analysis

## Climb is a best-in-class solution for *in vivo* drug discovery workflows

Climb's workflow engine is configurable to optimize work across therapeutic areas. Climb helps manage *in vivo* studies from colony maintenance through study design, planning, and data capture to sample collection and data aggregation.

Climb's task management tools allow scientists to choose from existing workflows or create new task templates as needed. Tasks and workflows are configured to provide appropriate levels of detail to ensure consistent and accurate execution by different technicians potentially working at different sites.

Climb's scheduling calendar tool allows tasks and workflows to be assigned to technicians and balance workloads across study teams. Technicians can utilize mobile devices and scanners to locate animals, conduct tests, and capture data more efficiently. Scientists can use Climb to retrieve the study data for input into their analytical tools for data analysis.

All activities and research communications are logged in real time and auditable with complete chain of custody for all tasks, workflows, and data capture executed within the system.

study design          workflow automation          sample tracking          scheduling

reporting          animal husbandry          veterinary care          data capture

# Managing Studies

Executing large studies can be an enormous logistical challenge. Many laboratories still rely on nonintegrated point-solutions and storing data in share folders. This becomes particularly challenging for large studies that involve collaborations with other research labs or CROs. Designing an experiment can often involve several roles, including study directors, 1 or more scientists, and lab/vivarium managers who need to communicate back-and-forth. Once finalized, these experiments need to be executed quickly, precisely, and accurately to analyze data for next research steps. Maintaining situational awareness on study progress and anticipating any hindrances is crucial to cost-effective and well-ordered study management.

## Challenges for managing studies

- Project management
- Allocating resources
- Creating easy to follow instructions for technicians
- Breeding animals for required research model
- Tracking progress
- Communications across distinct activity spaces and sites
- Aggregating, harmonizing, and delivering data



## Climb as a central tool for managing studies

Climb can be the communication and data conduit that unifies the various groups working on a study. Scientists and study directors can create and set up protocols in Climb, animal care takers and technicians can prepare necessary animals, and managers can assign staff to tasks and monitor study progress. All data generated in the study can be put into Climb, queried, and extracted for analysis- eliminating the need for a suite of disconnected point solutions, binders, and spreadsheets.  Climb also makes it easy to manage reporting for IACUC semi-annual inspections, AAALAC site visits, USDA inspections and external collaborators.

## *Use Case – Managing Studies at the UCSF IND*

A 50-person research group at the Institute for Neurodegenerative Disease (IND), under the directorship of Nobel Laureate Dr. Stanley Prusiner, partnered with RockStep to develop requirements and test Climb functionality for tracking animal breeding, genetic distributions, veterinary work, biological samples, experiments, screenings, data delivery, workflow, resource management and scheduling.  When the project started, the IND was committed to streamlining their workflows. They wanted to improve their research quality and reduce the expense of maintaining their aging technologies and homegrown systems. This collaboration with RockStep Solutions led to innovations that have helped make Climb a best-in-class solution for animal model research and drug discovery. Dr. Prusiner's lab now uses Climb as a single solution to manage their research program across a diverse group of scientists, technicians, and project

managers working at different sites and with collaborators at other institutions. Climb increased research efficiencies and quality that was previously being hindered by legacy tools and point solutions.

"We selected this company because many of the people in it have direct, hands-on, experience in other world-class animal programs, and we felt that they really understood our needs.

They have been very responsive to our requests, and we are appreciating the fruits of our collective hard work."

– Julian Castaneda, DVM, Ph.D.
    Director of Animal Facility, University of California, San Francisco

# Contract Research Organizations (CRO)

Research is often conducted by multidisciplinary teams working toward one scientific goal across distinct sites, often operating in different time-zones and countries. CROs commonly utilize email and cloud repositories, like Dropbox, as communication pipes to deliver messages and data. These tools are not designed for team collaboration, nor do they provide the level of desired security.



## Challenges for managing contract research organizations

- Real-time visibility into progress and laboratory activities across sites and studies
- Easy access to audit trails
- Client-defined security and data access controls
- Data wrangling
- Secure communication with clients

## Climb helps manage data and protocols for CROs

Climb solves the challenges of managing federated research by providing a secure platform for collaborative studies. As a native cloud application, Climb is a secure information bridge that spans geographical regions, time-zones, and international boundaries. Scientists at one site can create tasks and detailed protocols, then assign animal cohorts to studies that will be executed at a completely different site. Lab managers at the site of performance can use Climb to schedule activities while data analysts can access data in real time from anywhere. All participants in the study can have controlled visibility into the study progress and data. Meanwhile, IT departments do not have to manage access to data behind their firewalls, which may create institutional security risks and incur high costs. At the end of a study, all data and associated metadata are safely stored in one location for easy access.

> "Our lab conducts high throughput lab animal phenotyping and generates enormous amounts of complex data. We have high-profile research contracts with NIH and with leading edge companies. Reliable and accurate data capture, experimental reproducibility, and process control are crucial to our science. We tried a large on-premises LIMS, and it failed to meet our need to share data across multiple sites.
>
> RockStep Solutions stepped up to the plate with Climb, and their expert data wrangler team worked directly with our phenotyping team to help address our needs. Our lab now runs more efficiently, and we are getting more science done!"
>
> - Gary Churchill, Ph.D.
>   Professor Karl Gunnar Johansson Chair, The Jackson Laboratory

# Tracking Samples

Research labs often generate large numbers of samples that need to be appropriately stored, processed, and remain discoverable on-demand. A single sample may be used in several assays and are often shuttled between departments or institutions to be processed and analyzed by skilled specialists. The value of samples is limited by the quality of metadata associated with them. Climb's sample management capabilities associate each sample with the source of origin and study for which it was collected, while tracking sample movement through *ex vivo* and *in vitro* analyses to prevent loss and degradation that may impact data quality.

## Challenges for tracking samples

- Managing sample inventory
- Recording and updating sample location and status
- Tracking sample history and pedigree
- Tracking sample usage in experiments
- Allocating samples for various assays



## Using Climb for sample tracking

Lab managers are often tasked with sample inventory management. They need to know exactly what samples are in storage and how long they've been there, their exact location, how the sample was fixed, and who collected the sample.  Perhaps most importantly, scientists need to know the pedigree of samples and data associated with the samples, for example, protein quantitation.  Climb includes an integrated sample management module that makes it easy to manage sample inventory. Researchers can use Climb to locate samples and drill down to the details for a 360º view of a sample's history, pedigree, and associated data.

> "A big positive for us is that Climb is web based.  We can open it on a home computer or in the mouse room.
>
>  Previous databases kept all our information on one computer, and with Climb, we don't worry about out colony data getting lost if something happens to the computer.  It's always available."
>
> **– Julie Siegenthaler**
>  Assistant Professor, Department of Pediatrics, University of Colorado Denver

# Vivarium Management

Animal colony management is critical to *in vivo* research. It necessitates teams of various skills to ensure husbandry, facility maintenance, and scientific tasks are completed in well-ordered fashion. Animal rooms are controlled spaces that require special entry procedures based on regulatory guidelines. These requirements pose challenges to vivarium staff, such as PPE that restricts movement, making simple tasks difficult and lengthy. Communicating work plans clearly and making data entry easy improves the quality and accuracy of work and ultimately improves the efficiency of vivarium operation.



## Challenges for vivarium management

- Managing complex breeding strategies
- Timely weaning and separating animals
- Collecting samples
- Locating mice quickly and easily
- Spot checking cages
- Conducting strain census
- Conducting animal welfare checks
- Writing and reading cage cards
- Regulatory reporting

## Climb helps streamline work in the vivarium

With Climb, vivarium managers can create and schedule task lists that specify the level of detail needed for each task to be successfully accomplished. Tasks can contain instructions for any work activity, for example breeding, handling, moving, or genotyping animals. In Climb, each animal record includes detailed location information so the technician can find the animal quickly and efficiently. These animal records are used to easily generate animal welfare and usage reports. Technicians can use computer tablets, bar code scanners, printed cage cards, and RFID tags with readers to help automate their workflow. When a technician observes an animal in distress, a quick message can be sent to veterinary staff via Climb's internal messaging system, email, and SMS, allowing immediate decision making and initiation of treatment plans. Videos and photos may be included if desired.

> "Climb is user friendly, and it doesn't take very long to learn how to use it and there is a lot of support from the company to help with training. Along those lines, the customer support is awesome! Anytime we've had an issue, the support team is very accommodating and always handles our concerns in a timely manner. For example, we wanted customized cage cards and they were great about the design and making the cards available for us to access relatively quickly.
>
> We would highly recommend Climb for animal colony management and research laboratories."
>
> **– Julie Siegenthaler**
>   Assistant Professor, Dept of Pediatrics, University of Colorado, Denver

# Laboratory Animal Health

Animal health staff need to be alerted as soon as possible when an animal is in distress. Getting in and out of animal rooms is expensive in terms of staff time, materials, and added animal risk as well as disruptive to the regular flow of work. After diagnosis, a veterinarian may need to create a treatment plan for an animal. For regulatory compliance, treatment plans must be tracked and assigned to qualified technicians. Audit trails must be in place to ensure all animal treatments are conducted, and animal treatment notes are taken.

## Challenges for lab animal health management

- Timely reporting of animal health concerns
- Response time
- Locating animals for treatment
- Assigning and scheduling treatment plans
- Treatment resolution and reporting
- Auditable communication trails
- Regulatory Reporting



## Climb is the solution for laboratory animal health management

When an animal caretaker or veterinary technician observes an animal health concern, veterinary staff can be alerted immediately with SMS, emails, or directly through the Climb message center. Messages can direct staff to animal records with video or photographs, if allowed, of the distressed animal. Once notified, veterinary staff can respond immediately with treatment plan instructions or easily locate the animal to evaluate, armed with the necessary equipment and reagents as outlined in the information captured in the clinical observation record in Climb.

In addition, Climb makes regulatory reporting simple. Veterinary staff are able to pull detailed reports from Climb and, if an audit is conducted, Climb's audit logs track any information changes (add, edit, or delete), who made the changes, and display historical data associated with the record.

> **"[Climb is] drastically improving the operations of our Animal Care and Use Program"**
>
> **– Julian Castaneda, DVM, Ph.D.**
>    Director of Animal Facility, University of California, San Francisco

# Managing Resources, Activities, and Scheduling

One of the major challenges in running a research lab is assigning staff and resources to tasks. Veterinary staff and lab/vivarium managers have limited personnel whose time needs to be optimized to meet increasing demands. Space and equipment must also be reserved according to priority. Schedules and reservations may need to be altered at a moment's notice, for example if an animal requires emergency surgery. Managing resources, tracking, and scheduling effectively can be a daunting challenge.



## Challenges for managing resources, tasks, and scheduling

- Determining resource availability
- Over or underutilizing resources
- Communicating detailed tasks across distributed teams
- Sudden changes in resource assignment
- Real-time visibility into progress
- Audit trails
- Chain of custody

## Climb helps labs manage resources, activities, and scheduling

Climb has powerful scheduling tools to manage resources. The color-coded calendar views allow managers to assess resource allocation and schedule, or alter, accordingly. In addition, personnel are able to view their own task schedule easily. Assigned tasks can be configured to provide appropriate levels of detail to ensure swift and consistent execution by different technicians. Climb shows real time progress and upon task completion, Climb records an electronic signature for chain of custody reporting. Furthermore, groups of tasks can be time bound to create an experimental protocol, which can be compiled into a scheduled study to be executed on individual or cohorts of animals. Climb supports several different task types that are configurable to accommodate preclinical research across multiple disciplines. Schedules can even be exported as .ics files and imported to most calendar software.

> "Adopting Climb has improved our lab's efficiency and makes it possible to simultaneously manage multiple experiments, coordinate resources, and conduct complex protocols. In addition to having a great product, their support team is fantastic.
>
> Climb is clearly a leader in lab animal management systems!"
>
> **– Ron Korstanje**
> Assistant Professor, The Jackson Laboratory

# Regulatory Reporting and IACUC Inspections

Institutional animal care and use committees require that *in vivo* research facilities maintain detailed documentation on animal breeding, use, and protocol assignments. Researchers need to be able to provide detailed records of use as well as laboratory animal health records (diagnostic and treatment). For labs using paper or spreadsheet-based informatics systems, reporting is often a time-consuming and stressful process that detracts from executing studies and collecting data. Time is wasted through back-and-forth communications in an effort to gather information and clarify details.

## Challenges of regulatory reporting

- Locating detailed information on animal use
- Status of on-going studies
- Locating information about the status of animals waiting to go into studies
- Detailed records for chain of custody of tasks
- Tracking how many animals were used for a protocol
- Locating all animal health records

## Climb makes regulatory reporting easy

Research labs using Climb can easily prepare for annual regulatory reporting. With a few mouse clicks, they can report on all animals used or planned for use in a study. Reports include health status, what the animals were used for, who conducted the tasks assigned to the animal, and what the outcomes were. Our team is also able to create custom reports to accommodate your specific needs.

During regulatory inspections, printed cage cards with bar codes make it easy for inspectors to understand the connection between the physical world in the animal room and data in the database. Regulatory reports and inspections do not need to be massive, time-consuming operations if the database is up to date.

> "I just want to share my positive experience with you about Climb. Prior to using Climb, it was difficult to keep a perfect record on animal usage. It was always a pain when it comes to dealing with IACUC reviews.
>
> Since we started using Climb a year ago, we have had no mistakes in keeping records, and data entry is a breeze. During our protocol annual review a short while ago, IACUC had zero questions on our animal usage! Thank you!"
>
> – Mu Yang, Ph.D.
>   Director, Mouse Neuro Behavior Core, Institute for Genomic Medicine,
>   Columbia University Medical Center

# IoT Sensor Systems for Animal Labs

Researchers continue to struggle with experimental repeatability. The National Institutes of Health has expressed that experimental reproducibility is one of the two cornerstones of science[4]. Studies conducted with the same research models in different labs often produce inconsistent results. Being able to factor in and control for environmental conditions as experiments are conducted will help investigators develop better protocols. Noting any differences between studies or sites that may affect experimental outcomes can help guide better study design and provide more consistent results.

## Challenges for environmental monitoring

- Accurate data capture on parameters such as temperature and humidity that may affect experimental outcome
- Real-time access to data
- Correlating environmental conditions to study outcome
- Alerting to conditions outside of set acceptable parameters
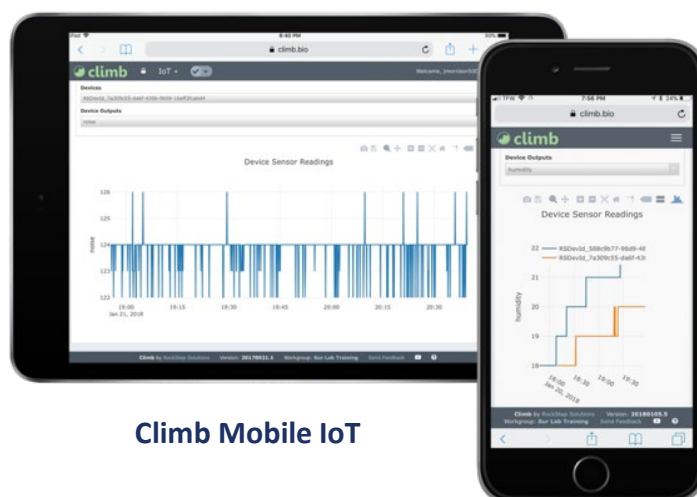


**Climb Mobile IoT**

## Climb integrates with Elemental Machines to monitor conditions in real time

Internet of Things (IoT) devices are now commonplace due to their significant computational capacity, powerful sensors, connectivity, and long-lasting batteries. With IoT systems, smaller is better and IoT devices are increasingly miniaturized- making them much easier to use in vivarium settings. In addition, machine learning algorithms can monitor IoT data streams, detect anomalous conditions, and remotely notify appropriate personnel.

Climb currently supports stream data from IoT devices built by Elemental Machines Inc (EM). EM's devices have sensors that measure temperature, humidity, pressure, noise, and light. EM devices are plug and play and can survive vaporized hydrogen peroxide sterilization for use in high health status barrier rooms.

Climb users simply register the devices and associate the data streams with the relevant database objects such as animals, rooms, or cages. Facilities managers and scientists can have access to environmental data over any time period and receive alerts in real-time if anomalous conditions are detected. Scientists can corollate the readings from the IoT devices with experimental data to better control the experimental conditions and reduce the number of experimental unknowns and potentially confounding variables.

# Advantages of Lab Informatics in the Cloud

On-premise solutions require expensive dedicated hardware, server rooms, security staff (physical and cyber), regular maintenance, and disaster recovery plans[5]. In contrast, cloud-based LIMS offer lower cost, mobility, scalability, better security, and centralization[5]. R&D IT is no longer defined as a suite of on-premise applications and services installed behind firewalls, run on servers controlled by local IT staff, and accessed via local area networks. Researchers now use applications and data accessed over the Internet and hosted on clouds and servers managed by different providers.

Information Technology for biomedical research is undergoing a rapid transformation as applications and data are moving into the cloud. According to the IT consulting firm Gartner, over 75% of all biomedical research organizations will have a cloud-first policy by 2019. The 2020 LIMS Market Research Survey from Astrix supported this projection, finding that 77% of surveyed companies currently use LIMS in their laboratories[6]. The utility of cloud-based LIMS was proven during the COVID-19 pandemic, which required rapid and precise methodology for international collaboration to produce an efficacious vaccine[7].

Software as a service (SaaS) solutions are simply licensed by subscription and meet the needs of the rapidly changing biotech and pharmaceutical landscape. With SaaS solutions, all the infrastructure, maintenance, updates, security, and disaster recovery systems are provided with the service. In addition, Cloud providers such as Azure, AWS, Google, and Salesforce, can provide the SOC 1 Type 2 audit reports required by many institutions where data security is a concern. The cloud provides elastic resources with nearly infinite capacity for growth, access to global infrastructure, and the most advanced technologies- including machine learning, artificial intelligence, mobile service, and geo-replication. Taken together, the movement into the cloud has matured considerably and rapidly, negating the majority of expensive and disjointed point solutions.

## Summary and Conclusions

Biomedical research is competitive. To stay ahead of the curve and remain profitable, organizations must become more efficient and improve quality with fewer resources. Digital transformation is one of the cornerstones for streamlining R&D processes. Modern digital systems can accelerate discovery, reduce costs, improve quality, and simplify IND submissions and regulatory reporting.

University research, while largely grant or foundation funded, is not immune to the economic pressures of improving quality while reducing costs. Grant funding is becoming more difficult to obtain and less dependable. Universities are relying more and more on sponsored research and/or are acting as CROs to improve their bottom line. Due to these increasing pressures, quality and efficiency are key performance indicators for both non-profit research and for-profit drug discovery.

Climb can be deployed as the core platform for digital transformation in any biomedical research organization. Climb manages research operations across the spectrum of research activities from the vivarium to the scientist's analytical work bench. Climb is customizable and flexible, allowing users to set up functionality specific to their role. Integration via API with other tools, such as electronic laboratory notebooks, is also available to help maintain a centralized and accessible data eco-system.

As a native cloud application, Climb is the platform for taking today's lab and transforming it into the Lab of the Future. Climb's simple subscription SaaS license model ensures you have a fast deployment, comprehensive training, and a smooth on-boarding. All application support, database backups, and security is provided by RockStep Solutions. Data are geo-replicated in real time, meaning you automatically have a disaster recovery plan included with your standard subscription license. Climb's global infrastructure is scalable and cost-effective for managing research collaborations, operations, and data.

For more information, please visit https://www.rockstepsolutions.com/ or email us at info@rockstepsolutions.com.

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