What Oncology Teams Should Look for in an EDC System

Most oncology teams are working feverishly to deliver medicines to patients quickly and safely, yet numerous inefficiencies slow them down. Advances in oncology need to be matched by advances in the clinical systems supporting those trials.

Immuno-therapies have advantages over traditional chemotherapy. They are less toxic, can address hard-to-treat cancers, and provide a durable response that in some cases lasts years after treatment ends.[1] They are also complicated to study as their efficacy varies in different settings, combinations, and treatment lines.

Research to maximize the efficacy of a treatment requires testing different combinations of drugs and different dosages, across different biomarkers. The resulting study designs are increasingly complicated, and the trend will continue.

> *More and more sophisticated trial designs are needed, especially for early phase and dose escalation trials, and often they'll need to be based on adaptive trial principles.*[2]
>
> – ***Pavel Tyan,*** *Advanced Clinical*

Adaptive trial designs, such as dose-finding, biomarker-adaptive, and treatment switching designs, are not new, however they present logistical and programming challenges that serve as an impediment to adopting these more efficient study designs.

For years, EDC technologies haven't kept pace with innovations in trial designs. Companies end up programming complex and fragile work-arounds because traditional EDC systems are unable to support their requirements.

This paper outlines common challenges when building databases for oncology studies and how a modern EDC equips you to build the studies you want, without limitations from technology.

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[1] Advanced Clinical, Trends in immune-oncology: Meeting clinical trial and market access challenges, 2020. https://info.advancedclinical.com/trends-in-immunooncology-whitepaper

[2] Ibid.

ONCOLOGY CHALLENGE: **COMPLEX STUDY DESIGNS**

Twenty years ago, when traditional EDC systems were designed, few companies were running the umbrella, basket, or platform trials of today. Each of these requires branching logic and adaptive design methods that aren't supported within traditional EDC systems, therefore clinical programmers create custom functions (programs written outside of the EDC) to add the necessary functionality.

Custom functions are custom code written by a programmer and each function can take from a few minutes to multiple hours to write. After they're written, you need to check their quality, which means additional test scripts and more UAT. We've seen some oncology studies that required over 300 custom functions.

Copying custom functions from one study to another saves time but introduces risk. Unless the study is an exact copy, any change to the structure of the study (folders, forms, fields, etc.) may affect the custom function itself and will require full re-validation in the new study.

Every custom function is a failure of your EDC to provide the functionality you need.

Reducing Custom Functions by 90%

Veeva Vault CDMS provides you flexibility within the system, not outside it. The EDC supports complex branching with simple rules and dynamics. Designers can easily define the branching logic in the rules engine to assign patients to the appropriate schedule based on their treatment arm – without custom functions. With rules and dynamics, fields, forms, visits, or even new cohorts can be added dynamically based on randomization data from an integrated system or data entered by a user.

Similarly, Vault CDMS supports cross-overs from one treatment schedule to another. Using rules and event groups, study builders can define and see what path the patient will take using a single schedule editor; whereas in traditional EDC systems builders needed different matrices to manage different schedules. In addition to being easier for the EDC builder, sites are assured they are seeing the right patients, even as patients are assigned or re-assigned between treatment arms.

The rules engine in Vault EDC also provides complex edit checks, cross-form edit checks, form linking, email notifications, and action statements (trigger questions) all without custom functions.

As a result, Veeva has reduced the use of custom functions by over 90%. In 2020, Veeva builds had a median of 2.5 custom functions per study, and many builds didn't require any custom functions at all. The resulting time savings enable programmers to build more studies and study teams to focus on critical matters such as patient engagement.

We are also working to minimize the need for writing rules in general. For example, we introduced a configuration tool for date comparisons. You simply select the dates and parameters and add range values. The system creates the edit checks to compare dates without the builder writing any lines of code. Similarly, none of the univariate edit checks (required fields, range checks, etc.) require programming. They are simply part of field properties and only require checking a box or providing the range.

By eliminating custom functions and minimizing the need for writing rules, Veeva is removing complexity from study builds and adding flexibility to better serve complex study designs.

EXAMPLE: REDUCING CUSTOM FUNCTIONS BY OVER 90%

Veeva performed an in-depth analysis of one customer's existing oncology study and demonstrated how to replace most custom functions with simple rules and dynamics.

303 Custom Functions within the Traditional EDC Could be Reduced to Three	
50%	Standard rules within rules engine
17%	Dynamics as simple rules
16%	Configured form links
4%	Email notification rules
13%	Could be replaced with three Java custom functions with Vault EDC

ONCOLOGY CHALLENGE: **TREATMENT CYCLES**

Building out treatment cycles in other systems can be a lengthy process as you need to pre-build visits for each unique treatment cycle. If there are two routes of administration and two dosing schedules that's four combinations times the planned number of cycles. It's not uncommon to build 200 treatment cycles in a study, each of which requires extensive QC and UAT.

Adopting a new system is a good time to re-evaluate your standards. New systems can introduce new capabilities or more efficient ways of working. You don't want to miss out on efficiency gains because standards tie you to dated processes.

Introducing Dynamic Cycles, Visits, Forms, and Fields

In Veeva's CDMS, we create dynamic treatment cycles, which can contain a superset of options, such as both routes of administration and both dosing schedules in the above example. We then use rules to specify which combination of variables to surface based on the patient. Patients in each cohort get the relevant visits, forms, and fields for their treatment protocol, and the study designer only needs to build one dynamic treatment cycle and a handful of rules. There are three enabling capabilities:

- Label over-rides allow you to specify names for each cycle instance. There is no need to build a net new cycle just to give it a unique name.
- Rules enable you to add dynamics based on cycle number, for example add forms A and B at cycles 2, 4, and 6 only.
- Configurable cycle counts enable you to extend the number of cycles by simply increasing the number of repeats. There is no need to build future cycles in advance or in an amendment.

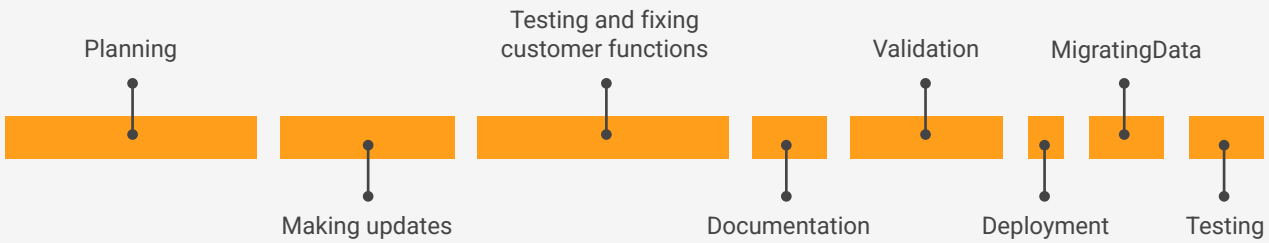
For typical oncology studies, programmers can expect to go from building 100+ treatment cycles in their traditional EDC to one-to-three cycles in Vault EDC. Using dynamics greatly reduces the UAT burden and increases confidence to meet First Patient In (FPI) targets.

ONCOLOGY CHALLENGE: **FREQUENT AMENDMENTS AND POST-PRODUCTION CHANGES**

A complex study can have numerous protocol amendments during its lifetime, each of which typically requires building a new database and migrating the data. Traditional EDC systems store data in a contiguous, linear manner. It is impossible to insert new data elements (fields, forms, visits) anywhere on that line except at the end, which isn't practical. The only way to fix this dilemma was to build a new study containing the new elements and migrate the data from the original study to the new one.

During a migration, the EDC will go off-line, meaning sites cannot enter data during that period. This is downtime, even if it was planned. As the diagram below shows, there are many factors contributing to the 8+ weeks it often takes to go live with an amendment in traditional systems.

A COMMON AMENDMENT PROCESS FOR LEGACY EDC SYSTEMS



Amendments with Push-button Deployments, Zero Downtime, No Migrations

Vault EDC can implement protocol changes with no data migrations and zero downtime for sites, even no planned downtime. Data is stored in a manner that provides flexibility and allows data managers to complete their work in the background, without disrupting sites.

Vault EDC's architecture also enables companies to host multiple versions of a casebook at any time, so each site is working with the most recently IRB-approved version. This enables your stats and medical teams to work with the most current and accurate data possible. Lastly, Vault has push-button deployments. Sponsors and CROs can deploy updates to sites in a matter of minutes instead of waiting for the vendor to do so.

How does it work? This brief **whitepaper** for technical and non-technical readers explains how Vault EDC supports multiple casebook versions and changes without any downtime or data migrations.

ONCOLOGY CHALLENGE: **LOCAL LABS**

The struggles of obtaining and managing normal ranges in a study are only half the issue; additional struggles come when normalizing results and units. While the industry has made advances over the years – most data managers and CRAs agree there are sharp edges on the process that should be addressed:

- Limited ability to override a normal range for one test
- Manual processes to identify impacted lab tests when a site forgets to provide updated ranges
    - » Limited ability to make the changes and reset impacted records for studies using the outdated range values
- Limited ability to store and reuse lab information for future studies
- Limited ability to normalize the results and units upon data extraction

Consolidating Management of Local Labs

Veeva developed an easy way to centrally manage local lab data including locations, normal ranges, analytes, and unit conversions. By using a single master list for all your studies, updating the master list once keeps every study current. If a reference range changes and there's a delay before making the update, Vault can **identify impacted lab results** and reset those records for each study using that lab.

The interface for sites simplifies data capture by automatically populating expected ranges and highlighting out of range data. And a separate list of unit conversions is used to automatically normalize lab results and units in your extracts.

Delivering the Innovations Necessary to Support Complex Trials

The methodologies for developing new cancer therapies are radically different than years past. With the emergence of affordable genomic sequencing, new highly targeted therapies have opened the field of precision oncology. The resulting need to test multiple therapies in isolation and in combination, and frequently in small patient populations, has driven the adoption of master protocol study designs.[3]

These complex study designs offer the promise to effectively test more therapies with fewer patients, thereby getting new treatments to patients faster.

Working with Vault CDMS takes the complexity and risk out of the EDC study build process, de-risking FPI deadlines and study amendments. If you're interested in greater efficiency, cost savings, and learning more about how Veeva can help you with your next clinical trial, please **contact us**.

[3] Seminars in Oncology, The Master Protocol Concept, 2015. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4681517/