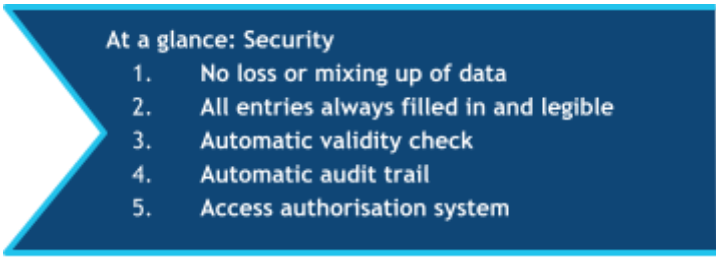
The 5 biggest advantages of eCRFs over paper CRFs

Digitalization has been advancing for decades and has evolved into much more than just a political buzzword – it has become reality in many private and professional areas. In an increasing number of everyday situations, paper had to give way to modern electronic solutions: Young drivers have never seen a printed roadmap and the idea of mailing a printed order-form accompanied by a check to Amazon appears absurd. But surprisingly, in the field of clinical trials, paper is still being used in some places to document the results!

In the following, we will briefly discuss the five biggest advantages of electronic case report forms (eCRFs) and why paper should no longer be used in clinical trial documentation.

1. eCRFs are safer



Clinical trials take place in a highly regulated environment. GCP, MDR, IVDR, 21 CFR 11, GDPR, etc. ensure that the integrity and data protection of the patients is guaranteed and the data quality is ensured. Great efforts are made to minimise risks of mix-up, loss or inconsistency of the data set, thus ensuring that reliable and medically valuable data are generated in the end. Nevertheless, it is not unheard of that even big research projects come under criticism or even fail because of problems with data quality.

When using paper-based case report forms (CRFs), there are various sources of errors that cannot be completely eliminated:
In the worst case, individual CRFs get lost entirely. Fortunately, this is quite rare, but it does happen, occasionally. Far more often, errors occur during subsequent handling and processing of the CRFs. Especially during data transcription from the questionnaire to the database (or less ideal – an Excel sheet). The gold standard here is independent double entry with subsequent comparison. That way, transcription errors can be detected and, ideally, corrected. Data transcription is a repetitive and uninspiring task that requires utmost concentration, so it is hardly surprising that mistakes creep in, regularly. Seemingly small errors, such as transposed numbers, slips off the line or plain typos can have a big impact if they go undetected.

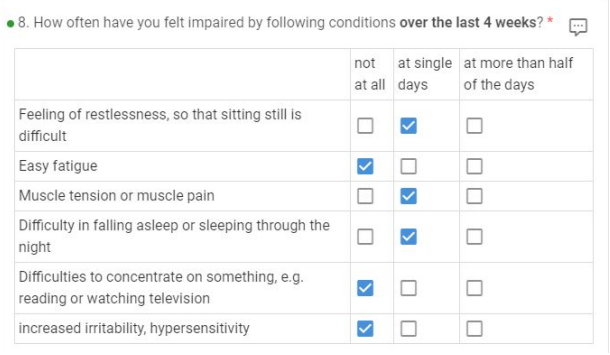
Another cornerstone of every study is that data can always be clearly assigned to a patient, in a pseudonymized fashion. This is usually achieved by means of an identification number, which is either handwritten on the CRF and into the ID-log (which decodes the real patient name) or by using two identical pre-printed ID-stickers. Of course, hand-written IDs are

prone to spelling mistakes and legibility issues. And even stickers can end up on the wrong form or in the wrong row, accidentally – especially if a large number of subjects are being processed at the same time. These errors should not actually happen, but they do occur in reality.

With electronic CRFs (eCRFs) patient and data management is handled automatically, all data goes directly into one database without an intermediate step of manual entry. This eliminates the possibility of transcription errors or patient mix-ups.

Another problem with paper-CRFs is ambiguity and poor legibility of the answers. It is particularly problematic if the handwriting is misinterpreted and thus wrong information is taken over into the evaluation. However, handwriting is not the only problem. In case of free text answers, multiple synonyms or paraphrases may exist that describe the same diagnostic finding. For example, the terms "obstructive lung disease", "hyperresponsive bronchial system", "bronchial asthma" or "asthma" can describe the same situation. This complicates data collection and interpretation and can lead to incorrect entries and, in the worst case, incorrect conclusions from the study.

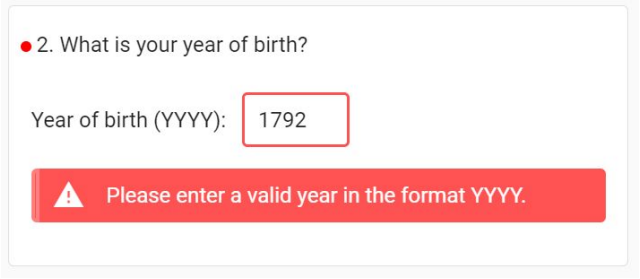
But it doesn't even take complex medical terminology to create ambiguous situations. Even a simple checkbox can be checked in an ambiguous way, on paper: People use crosses, check marks and other signs not quite in the box, cross out their original answer, correct their answer or check multiple boxes where only one is allowed. Now it is unclear how the answer is to be interpreted. That leads to unnecessary additional work in the form of queries and, in the worst case, incorrect data.


8. How often have you felt impaired by following conditions **over the last 4 weeks**? *

	not at all	at single days	at more than half of the days
Feeling of restlessness, so that sitting still is difficult	☐	☑	☐
Easy fatigue	☑	☐	☐
Muscle tension or muscle pain	☐	☑	☐
Difficulty in falling asleep or sleeping through the night	☐	☑	☐
Difficulties to concentrate on something, e.g. reading or watching television	☑	☐	☐
increased irritability, hypersensitivity	☑	☐	☐

Electronic questionnaires, on the other hand, are always legible, boxes are clearly ticked/unticked and comments are in designated fields. Predefined Answers in drop-down menus or selection lists enforce consistent terminology and spelling, thus facilitating data interpretation and preventing incorrect/inconsistent entries.

With paper CRFs, however, early error detection is hard to impossible, some mistakes are easy to spot, for example, it is rather unlikely that someone was born in 1399 or takes 44 tablets of a heart medication every day. But other errors are much less obvious and evade detection, even when reviewed, carefully. Again, there is the danger of incorrect data making it into the database and hurting the quality of your study.



In an eCRF, validity criteria can already be defined when the question is drafted, which checks directly during input whether the answer is within a plausible or required range. This prevents avoidable queries and incorrect entries.

In addition, the electronic system offers further advantages to minimise risks that are not technically feasible with paper:

For example, electronic CRFs typically have an automatic audit trail in which every single entry or change is logged with a timestamp and the ID of the person making the change.

Electronic questionnaires are also far ahead of paper questionnaires when it comes to data protection: electronic authentication and permission systems guarantee that only authorised persons or groups have access to the data they are supposed to work with.

Many of the errors can certainly be caught or mitigated by a stringent query process. However, this not only costs time and money, but despite all the measures taken, some level of problems certainly remains.

2. eCRFs save working hours

Both the paper questionnaire and the electronic version have to be created, filled out and evaluated. But as described above, some additional work has to be done when using paper-based questionnaires: Paper questionnaires have to be printed, collated and mailed to the study centers. The completed paper forms must then be scanned, filed, and transcribed into the database using double-entry and review. Each work step and change of media bears another risk of error and additional work, resulting in additional costs.

At a glance: Work efficiency

1. No additional input into a database
2. Fast completion because only relevant questions/CRFs are displayed
3. Faster query management
4. Automatic dispatch

With an eCRF, all these additional steps are unnecessary. After the eCRF is created, all data automatically goes to the database, where it can be reviewed and evaluated, easily. No transfer between disconnected systems is happening.

Furthermore, paper is not well suited for sophisticated navigation of the questionnaire: some questions may only be relevant to a subgroup of the cohort and depend on the answers to previous questions such as age or previous disease. The only way to handle this, on paper,

is to include instructions to skip some questions if certain conditions are fulfilled. These are easy to overread or get wrong, turning the process into a scavenger hunt.

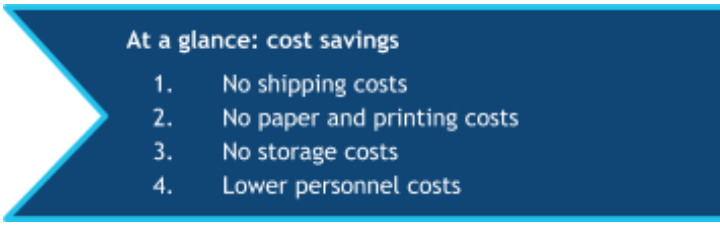
In an eCRF, questions can be configured so that they only appear depending on a previously given answer. For example, it is easy to only include a question on pregnancy if the participant is female according to a previous item. This makes answering the questions much clearer and faster.

Last but not least, when more than one centre is involved in a study, sooner or later ambiguities arise that need to be sorted out in queries. These queries and their resolution have to be documented in a comprehensible way. For paper CRFs, this means entering corrections without making the original entry unrecognisable, manually documenting and countersigning each and every step.

In an eCRF system, queries can be easily submitted and answered within the system. The documentation happens automatically without any additional effort and a complete audit trail ensures traceability.

3. eCRFs save costs

The use of paper CRFs not only results in higher labor costs. Other costs also incur: We have already discussed things like printing, handling and shipping, above, but all these documents must also be stored, safely for extended periods of time in order to be in compliance with applicable regulations.



These additional costs can be reduced to essentially zero by using electronically based eCRF systems.

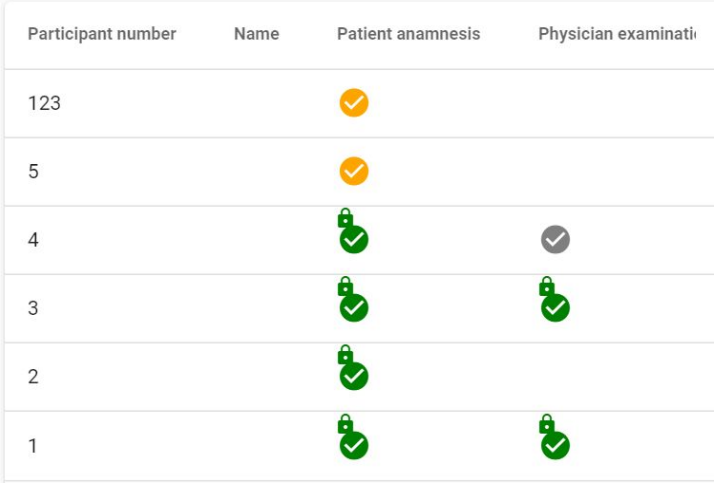
4. eCRFs are more user-friendly

At a glance: user-friendliness

1. Overview of progress
2. Questions/answers in language of choice
3. Different font sizes possible

In many studies, CRFs cannot be filled out completely at once: Lab reports or further diagnostic procedures may still be pending or, in longitudinal studies, the results of several visits flow into one CRF. If the study is conducted on paper, it is time-consuming and difficult to keep track of the processing status of each individual form and/or patient at all times. However, this information is a central element for the successful monitoring and management of your clinical trial. What is my recruitment status compared to the plan? What does this mean for the completion date? How many queries are still open? How quickly do you expect to be able to close them? Which subjects still need to be reminded to return a form, or need the follow-up survey, now? These are all important parameters in study management that demand a lot of care and effort from those responsible.

When using eCRFs, the study team always has a complete overview of the processing status of each CRF and the status of the study as a whole.



Especially in international, multi-centre studies, the same questions have to be asked in all centres – often in the local language, e.g. for patient reported outcomes or if the local study staff does not have sufficient knowledge of English. When transcribing the data into the database, the processor must either have the appropriate language skills or assign the questions by their numbers because he does not understand the question text. This can quickly lead to misclassifications.

Unlike paper questionnaires, with eCRFs the language of the questions can always be selected in the system, so that each study centre uses the CRF in their own language. Transcription is unnecessary and the study director can view, check and evaluate the database in his or her own language. Only free-text responses may require translation. In this way, language barriers are overcome and international multicentre studies can also be conducted without linguistic friction and sources of error.

The readability of the questions is also better with an eCRF than with paper, as the font size can be enlarged and reduced, as is common with all modern internet sites. This is particularly beneficial for participants with impaired eyesight or when working on small mobile devices.

5. eCRFs are more sustainable

Nowadays, it is more important than ever to use the resources of our planet, wisely. Electronic questionnaires, of course, do not consume any paper. Even if you only have a small study with a one-page questionnaire: it is not the only study of this kind and so many tonnes of paper can be saved across Europe by using electronic questionnaires.
Furthermore, the questionnaires do not have to be sent out and stored. Above all, this has a positive effect on the carbon footprint: the statistics of the International Energy Yearbook 2015 showed that sending a single letter produces a total of about 20 grams of CO_2, whereas sending, opening, reading and answering an email produces a total of significantly less than 10 grams of CO_2.

Paper questionnaires in clinical studies are certainly not at the top of the list of environmental offenders, but if it is so easy to make a contribution to environmental protection at this point, one should also take advantage of this opportunity.

Summary

Rationally, there is actually no good reason to hold on to paper CRFs, other than habit. Electronic solutions not only provide an adequate replacement, but offer numerous advantages over traditional paper documentation – they make work easier, speed up the process, create transparency and increase data quality. This leads to cost savings with better results at the same time: Win – win.