Authorization Codes

As Sponsors look to leverage technology in clinical trials to help maintain and control adherence to the design, methodology and all aspects of a protocol, they are often left with only two functionality options to control potential protocol deviations. They can leverage Soft Stop functionality where a warning message is shown, providing information that may change the end user's course of action but can be ignored or overridden with only minimal action, such as a checkbox acknowledgment. Alternatively, they may also leverage Hard Stop functionality where the end user is either prevented from taking an action altogether or allowed to proceed only with the external override of a third party.

Soft Stops can be useful for protocol deviations that may be a minor violation. For example, missing a visit window because the subject was traveling may not be as severe as a protocol violation where we need to prevent the action from being taken all together. Providing the end user with a Soft Stop warning, and generating a notification of such deviations, allows the end user the proper guidance and discretion to choose how to proceed, while giving the Sponsor appropriate oversight of these deviations.

Hard Stops can be useful for protocol deviations that may be a major violation. If a visit window is in place for safety reasons, it makes sense to always prevent the treatment visit from taking place outside of the window.

Challenge

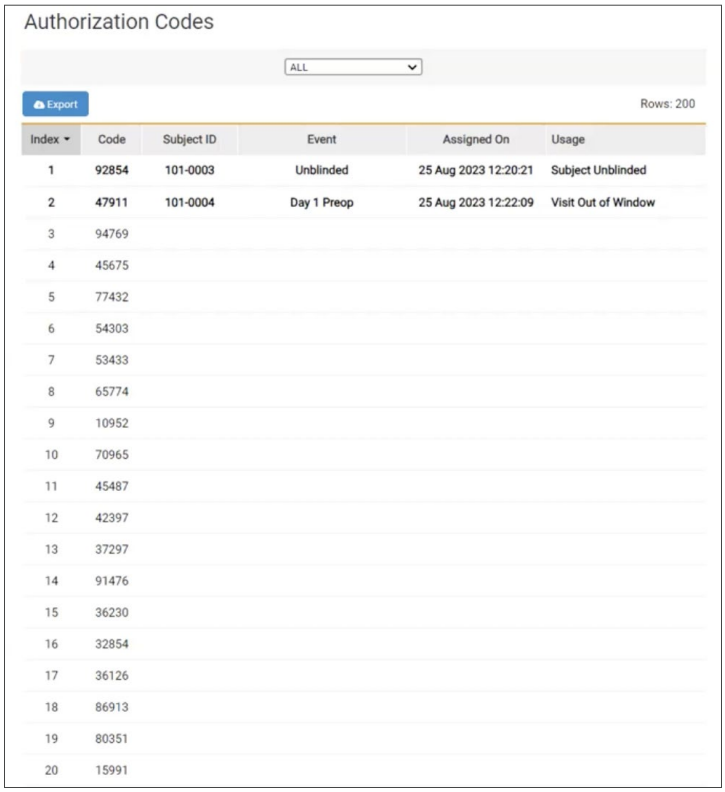
Sometimes scenarios may not fall exactly into these two buckets. There is the potential for protocol exceptions, where a single patient, or a small group of patients, are allowed to deviate from the protocol as a temporary measure that is pre-approved by the Sponsor or funding agency and the IRB, prior to its implementation. There is also the potential that what would be a minor protocol violation on its own, could be a major violation if it occurred multiple times, like out of visit windows. Sponsors may want to use Hard Stops to help review each occurrence and ensure all factors are considered before approval.

Third party expertise is not needed in these scenarios, so having to communicate and update to additional team members can add time to completion and increase the likelihood for potential errors in the transfer of information and process. Sponsors often need a process that bypasses third parties to ensure a more streamlined and quicker approval.

Solution

Authorization Codes are a predefined numeric code that is only allowed to be used once during the life of the RTSM study, to override a Hard Stop. A list of authorization codes will be given to the agreed upon study team users (roles) who will be responsible for issuing codes to the designated end users when appropriate. This code is entered by the end user role during a transaction in the RTSM, to allow the user to bypass the Hard Stop.

The list of authorization codes will be updated with any details of historic use, as well as presenting unused codes. This process will be part of operations and sites will receive training on who to contact, when and why. The best practice is to provide multiple people with access to the authorization code list for redundancy.



Index	Code	Subject ID	Event	Assigned On	Usage
1	92854	101-0003	Unblinded	25 Aug 2023 12:20:21	Subject Unblinded
2	47911	101-0004	Day 1 Preop	25 Aug 2023 12:22:09	Visit Out of Window
3	94769				
4	45675				
5	77432				
6	54303				
7	53433				
8	65774				
9	10952				
10	70965				
11	45487				
12	42397				
13	37297				
14	91476				
15	36230				
16	32854				
17	36126				
18	86913				
19	80351				
20	15991				

Authorization code overrides can be applied to the following areas to create an approval process between the site and the Sponsor/CRO:

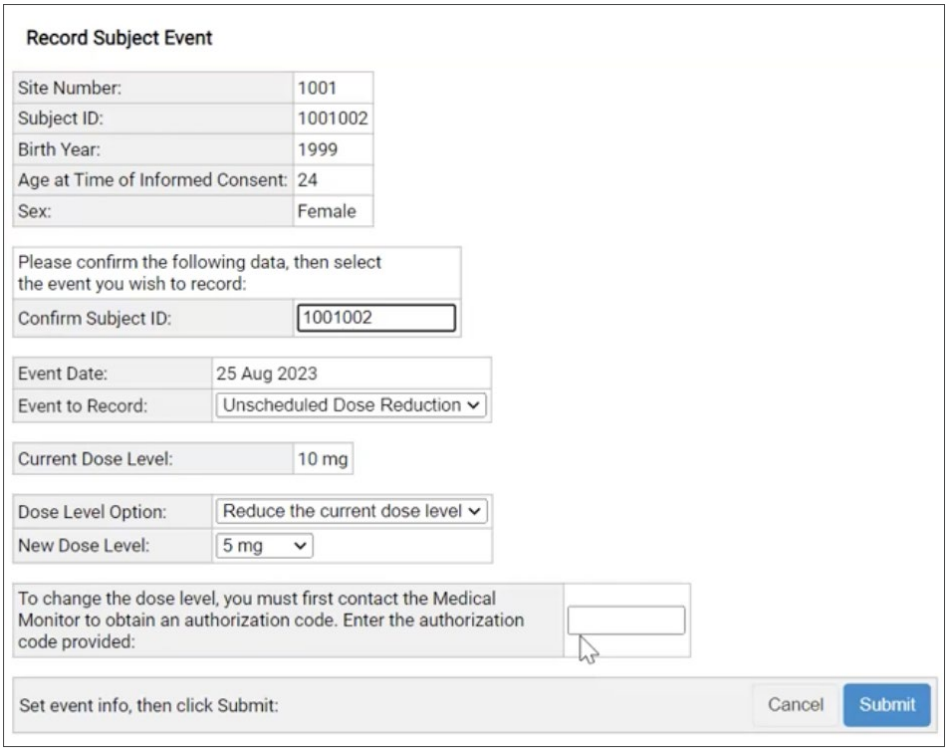
Eligibility Not Met – Allow a subject to proceed despite not meeting all of the Inclusion and none of the Exclusion criteria.

Out of range Age – Allow a subject to proceed despite not meeting the normal age validation range for the study.

Out of Window Visits – Allow a visit to be taken out of the normal window.

Titrations – Allow a change in a subject's dose level.

Unblinding – Allow an Unblinding transaction.



Conclusion

Authorization codes can present a happy medium between Soft Stop and Hard Stop functionality to ensure there is an appropriate pause, review and approval process that bypasses a third party. This creates a streamlined process that ensures approvals can be quickly turned around, while giving the Sponsor the correct opportunity to review and provide the correct decision on a case by case basis. Reporting of historical overrides allows the Sponsor to review past approvals and take any earlier decisions into consideration if needed.