Abstract
Clinical trial participants retain 30-48% of informed consent information and 44-57% understand components of studies, including procedures and major risks. Given the complexity of first in human stem cell interventions and limited information on the long term effects, investigators may wish to exceed the minimum elements of consent in order to ensure patient self-determination and to increase their safety. Recent FDA guidance recommends facilitating consent electronically to enhance such understanding of the trial risks and to increase retention and comprehension of information which may lead to an increase in protocol adherence. Enhanced electronic consent (EEC) may include many types of media, and including multimedia has been shown to significantly increase understanding by 31%. Likewise, enhanced consent has been shown to significantly increase comprehension by 41%. To achieve these goals in such novel studies, the UC San Diego CIRM Alpha Stem Cell Clinic is piloting this implementation. We present our process.

Our site designed EEC that is delivered via iPad tablets and uses free software. Validating electronic participant signatures is complicated by stringent federal regulations, so our method supplements the paper form (participants continue to sign paper). Beyond an enhanced consent document, we offer interactive educational e-books covering basic clinical trial information and a stem cell primer, including content from ISSCR.

Introduction
We sought a medium to more easily convey clinical trial information and to make it digestible to patients. This would ideally increase patient understanding and adherence. Our goals were to determine key elements to include in this enhanced consent, including general education and features of an enhanced consent. We then sought sources for such content with an emphasis on keeping costs low. The final product was tested with patients.

Materials and Methods
Platform & Software Selection: We chose an Apple iPad Pro 13" tablet because its large screen enhances readability without sacrificing portability. Software was selected based on design capabilities, ease of use by staff and patients and by cost. Apple iBooks Author was selected for designing and publishing books. Apple iPad tablets, combined with an Apple Keyboard and Apple Pencil device were selected to facilitate interaction with the EECs and EEMs.

Essential Elements: We identified the key elements of an enhanced consent or educational material (table below) using literature searches; discussions with physicians, coordinators, a genetic counselor, and staff from other CIRM ASCC sites; and from anecdotal patient reports.

Content Selection: We explored existing credible resources and meritorious groups with scientific and patient-centered focuses for each content area: the enhanced consent, Clinical Trials 101, Stem Cells 101, and CLL information.

Patient Interactions: Before officially deploying, a small number of patients in our multispecialty oncology clinic were invited to browse the iPad content and to provide anecdotal feedback about their experience with the iPad tablet and its content. Patients required little or no instruction for use.

Results
Ultimately our partnerships and process produced 5 books across 2 months: 2 EECs and 3 EEMs on clinical trials. Forging strong collaborations allowed us to produce credible content while minimizing cost. Selection of free software also limited the cost. We partnered with ISSCR and Youreka Science and also used freely available content from NIH and UCSD libraries in order to produce credible, understandable and interactive elements. ISSCR provided information for a Stem Cells 101 EEM while Youreka Science allowed use of and minor editing of whiteboard videos. These videos, embedded into EECs and EEMs, describe CIRM-specific trials and diseases in lay-terms with an appropriate degree of scientific discussion. Library content is used to produce disease information for newly diagnosed patients or those who wish to learn more. In every case, attribution of the source is given including links so that patients can learn more at home.

Future Directions
Further discussions led us to explore a version 2.0 which will enhance the digital exporting of annotations for use by patients and for analyses in order to improve future enhanced electronic consents. Due to restrictions in the Apple iBooks Author software and iPad iBooks reading application, we will develop future EECs and EEMs using Adobe Creative Suite software. Adobe InDesign is the primary means to affordably design and publish materials which can be read by existing, free software on the iPad. We will also develop a statistical plan to measure knowledge and comprehension.

Pending results, especially after analysis of patient annotations, other sites may wish to use our process in order to increase patient understanding and comprehension particularly of study risks, benefits, procedures and to discern myths and truths in stem cell research. Our cost-effective process may lead to increased accrual, higher adherence, fewer deviations and overall improved trials.

References

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Enhanced Electronic Consent (EEC) and Electronic Educational Materials (EEM) for Stem Cell Studies May Increase Protocol Adherence