

Report on EVADO prepared by:

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**Dr. Sudhir's biosketch:**

The author of this report, Dr. Sudhir is a physician and cardiologist who heads a Global Clinical Science group at Abbott Vascular, Cardiac Therapies in Santa Clara, CA, and is responsible for the development of worldwide strategies for clinical research in drug-eluting stents and newer technologies. My team oversees clinical research over a broad range of interventional therapies in areas that include early R&D, clinical development, post-marketing studies, publication strategies and women's health initiatives.

I have previously held senior clinical positions in the biotech industry including Executive Director, Clinical Development, at one of the Johnson & Johnson Internal Ventures in Mountain View, CA, Vice President of Medical Affairs at diaDexus Inc, South San Francisco, Director of Clinical Development at Millennium Inc, South San Francisco, and Director, Cardiovascular Research at Pharmacyclics Inc, Sunnyvale, CA. My industry career spans a broad range of experience in drug and device development, and I have overseen clinical trials from phase I and first-in-man studies, through product approval, as well as post-market trials in multiple geographies worldwide.

Prior to joining the biotech industry, I worked for over a decade in academia, holding various positions including Associate Professor of Medicine at Monash University; Consultant Cardiologist at the Alfred Hospital, Co-director, Hormones and Vasculature Research Laboratory at the Baker Heart Research Institute, Melbourne, Australia; Director, Vascular Research Laboratory, and Assistant Professor of Medicine, Cardiology division, University of California, San Francisco (UCSF).

During my academic career, my major contributions were initially the fields of hypertension and atherosclerosis, and subsequently in the application of intravascular ultrasound and Doppler to the study of coronary vascular physiology. I have also published extensively on the actions of sex steroids on the cardiovascular system.

I have an MD from the University of Madras, a PhD from Monash University, Melbourne, Australia, and a cardiovascular fellowship from the University of California, San Francisco. I have served as a principal investigator on clinical trials and preclinical studies, as a speaker on regional, national and international academic and pharmaceutical lecture circuits, and as a member of scientific advisory boards. As a physician and cardiologist, I have practiced medicine and conducted clinical trials globally, and am a Fellow of the Australian College of Physicians and the American College of Cardiology.

I have published over 100 academic papers in peer-reviewed journals, and a dozen chapters in medical textbooks. I have served on the Editorial Board of the Journal of the American College of Cardiology, and continue to be a reviewer for several journals and academic bodies. I am also a Consulting Associate Professor of Medicine in the Cardiology Division at Stanford University.

### **Overview of Evado:**

Evado is an Australian company that produces clinical trial software to capture study information. The product is an e-CRF (electronic case report form) that replaces paper. The web based software allows for designing, collecting, and of course storing data. Additionally, the important aspect of trial safety data is provided as an online feature. There is certainly a need, both in the pharmaceutical and medical device environment, to have lighter versions of e-CRFs. This would be particularly appealing to small and medium size biotechnology and biopharmaceutical companies, where the need to run low cost clinical trials is critical. The software addresses the requirement of 21 CFR part 11 in terms of being a closed system, system validations, the ability to generate accurate records, read records through their retention period, limit access to the system, record audit trails, authenticate and identify all users, provide personnel training, and use of appropriate document control.

### **Evado's specific features and functions:**

Evado is a low cost, user friendly alternative to more expensive clinical trial software packages. The CRO can directly capture the CRF content online using a standard web browser. Functions and features include the following: web based trial record form editor, field record form, central record form repository, standard lab test management, and online analysis of trial records outcomes. I believe this functionality provides the essential features required by most end users.

There are a number of specifics of note, relevant to its application to registration trials:

- User activity is logged at multiple levels in the application
- Evado has audit trails covering the content on all forms. The audit trail consists of a DES3 encrypted difference table containing the old and view values of all fields that have changed.
- Identifiable patient data is DES3 encrypted and only the users at that site are able to see the data in a clear state.
- Evado provides both single and double token signoff. The user's tokens are authenticated against the user's credentials in the Active Directory service.
- All records use token signoff when a user is signing off a record, e.g. the author completes a form, a form is reviewed or a monitor raises a query. All signoff's are logged in the server log, the database log and in the form being signed off.

- All form field queries are annotated at a field level and summarized at the form record level. A copy of the queried record is made showing the record state when it was queried. The record author is alerted to the query and can access the queried record to address the query issues. Record reviews, data manager and monitors can query records.
- Role management is used to control user's access to menus, pages and forms and the commands or processes a user is able to initiate.
- Site users access is restricted to accessing only those subjects at that site in trials the user has a minimum of reader access to.
- The form design tools let users design both CRF pages and common forms like AE or SAE forms. Evado contains a set of standard validation rules for each form field data type that can be enabled using the form design tools. This lets investigators design forms without the need to know or understand how write software or validation scripts.
- Forms layout templates are automatically versioned, the versions increment when a form is saved or issued.
- Evado form management system allows data managers to revise form design during the trial to add a new field. The form record management process links each record uniquely to the version of the form layout that generated the record. When a new form is issued, records generated new version will have the fields in the new form and any records created with the previous version will have the fields in that version of the form. Once a form layout has been used to create a record, none of the fields on that form layout can be deleted.
- The data dictionary lets the data manager control the form field naming conventions and associated validation rules to be used on that field.
- The regulatory report generation function lets users create regulatory report like a CIOMS form using a standard Evado form layout, once the form has been reviewed it can be displayed using a CIOMS form layout.

**Recommendations:**

Having performed a detailed review of the software, it is my opinion that Evado's software would be extremely attractive to both biopharmaceutical and medical device companies. It can be readily used for a range of Phase I and II, through to Phase IV trials, and would be appropriate for both First-in-Man as well as pivotal medical device studies. Data obtained using this software would be acceptable in submissions to the US FDA, in view of the features described in detail above. In recent years, as both the drug and device sections of the FDA has been very open to clinical data collected in Australia, I have personal experience of submitting such data, obtained using Australian software, to the FDA. While Evado's forms do not resemble Phase Forward's forms, or those from other vendors, they have been designed to make them easy for researchers to fill in, and optimize download time and data integrity. The vendor has the capability to work closely with the client to tailor-make the software to individual requirements, incorporating features such as ECG capture and imaging data that may be specific to a particular trial. I have no hesitation in recommending this software to any company seeking to use it in the pursuit of approval of a product by a regulatory body such as the US Food and Drug Administration.