



As the Managing Director of Veeda Clinical Research, I would like to personally thank you for your interest in our quarterly newsletter, **The ANDA Pulse**

If you are an existing client, we thank you for your continued business and support. If Veeda has not had the chance to work with your company, I welcome the opportunity to learn more about you and the chance to earn your business.

Veeda's business mission is simple: to support our clients in maximizing their potential and meeting their business objectives. Our goal with this newsletter is to help keep you informed on the developments within the Veeda organization and on the important issues that impact our ever-changing industry. We hope that this information will be useful in your business endeavors and that Veeda can play a more integral role in your clinical research initiatives moving forward.

We have put together a one of the best teams in the industry to meet your needs. Vincent Scamacca is our Business Development Executive and your point of contact here in the US. In India, Veeda has a group of highly skilled clinical, bio-analytical and project management teams to handle your studies once a study is initiated.

Veeda understands that execution is key and that delivering FDA quality data and meeting your timelines are essential when developing new formulations or trying to be the first to file. We are committed to delivering results and would welcome the chance to play a role in your drug development efforts as a research partner!

Once again, enjoy the newsletter and I look forward to the opportunity to work with you!

Apurva Shah  
Group Managing Director  
Veeda Clinical Research

### Veeda is your Pulse on news effecting your ANDA submission

Veeda Clinical Research brings you the ANDA Pulse, a quarterly newsletter focused to help you with your generic drug development and ANDA submissions. The ANDA Pulse will be loaded with news on all aspects of information related to Global regulatory laws, the changing face of generic drugs, the Hatch Waxman act its implications, proposals at various important forums like the USFDA, MHRA and the DCGI. This Newsletter will be delivered to you in an electronic format in your emails.

Veeda Clinical Research is a renowned CRO conducting Bio-equivalence studies which brings to you updates on the "generic" front. Veeda Clinical Research is the only Anglo-Indian CRO which brings to you the Generic "Recall" free of cost. This is one of the first editions of the Generics Newsletter & we look forward for your continued faith and support that you have the Veeda CR BA-BE services. ●

### Veeda in Focus

Veeda Clinical Research is India's largest and most experienced Phase 1 CRO specializing in the early clinical development of drugs. With state-of-the-art Phase I facilities in India and the UK, fully accredited GLP Laboratories, and an established Biometrics team in both Belgium and India, Veeda CR is able to provide our clients a full range of phase I and IIa services.

Veeda has completed over 600 studies including over 270 bio-studies for major pharmaceutical companies worldwide. We have been audited by several of the world's leading regulator bodies including 4 times by the USFDA. Over 130 of our complete studies have been for USFDA submission with over 30 of them being FDA ANDA approvals!

Veeda was awarded the Frost and Sullivan's "Partner of Choice" for phase 1 studies in 2007 and has earned the trust and business of several of the world's leading pharmaceutical companies. Veeda understands Phase 1 Research and has the type of expertise you need in a CRO partner to assure you study is done right! ●

### Quick facts about Clinical Studies in India

- India is fast becoming one of the preferred countries to conduct clinical studies with an estimated 5% of all studies being conducted in India by 2011.
- Gujarat (Veeda's home state) is India's largest pharmaceutical business hub because of its highly educated and trained workforce.
- Today's Indian regulatory framework is compliant to international standards in areas such as Good Manufacturing Practice and Good Laboratory Practice.
- The FDA recently set-up an office in India. ●

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## The ANDA Pulse

Summer 2009

### We Know BE/BA

Veeda Clinical Research is a leading Indian CRO which conducts Bio-equivalence (BA/BE) studies for the Pharmaceutical drug companies. Veeda has expertise in all therapeutic areas of interest but has an exclusive niche in handling Bio-equivalence Studies for the Anti-retroviral Category of Drugs.

Veeda has completed over **650 Studies** for both major Pharma and Generic clients. A sampling of our study history includes:

- 150+ Pivotal BE Studies for US **FDA** submission conducted in India.
- 30+ Pivotal BE Studies for UK **MHRA** & **EU** submission
- 38+ studies being **FDA ANDA Approvals!**

Veeda has been audited by several of the world's regulatory agency including **4 times by the USFDA!** ●

### India is Popular for Early Phase Studies

There are good reasons why India has become so popular for early phase clinical studies with Western pharmaceutical companies. Trials may be 40% to 60% cheaper to run in India than they are in the United States or Europe, but there's more to it than simply cost. India has a very high patient-doctor ratio, and there are more English-speaking doctors in India than in the United States. Add to that an excellent IT infrastructure and a huge patient population (over 1 billion and growing)—the majority of whom are drug-naïve—and it becomes clear why the number of trials carried out in India is growing rapidly.

According to consulting firm McKinsey, the number of clinical trials in India totaled about \$340 million on less than 2% of the global clinical trials in 2008. But according a new research report by RNCOS, a number of factors such as low cost, large patient pool, easy recruitment, strong government support and strengthening of its intellectual property environment targets India's clinical trial market between \$1.5 - \$2 billion on nearly 5% of the global clinical trials by 2012. ●

### Generics remain a high growth industry

The generics market remains a major growth area in the global healthcare market. That growth has been partly driven by cost-containment in several national healthcare sectors and with governments seeking to promote the use of generic products over higher-priced originator products. The global generic pharmaceuticals market was worth over \$100bn in 2007, with market growth noticeably higher than that of the overall pharmaceutical market.

Generic prescription volumes have consistently exceeded those of branded prescriptions and this trend is likely to continue during and beyond the forecast period (2007-2013). A rapidly aging population in the United States is another key reason for the growth of generic prescriptions.

The market is expected to get a strong boost with the patent expiry of several blockbuster drugs in the next five years and also with the launch of biogenerics (expected in around 2010). Patent expiries of blockbuster drugs and the availability of multiple low-cost versions of these drugs have had a significant impact on generic prescription volumes, which rose from 48 to 57.3 percent during the same period and are likely to increase further to 77.6 percent by 2013.

Overall, the unbranded generic market is expected to continue its double-digit growth rate between 2007 and 2011 and generate revenues worth more than US\$ 69 Billion by 2011. ●

### Blockbusters that are losing exclusivity in the US

Blockbusters – drugs with \$1 billion annual sales or more - constitute the “backbone” of the pharmaceutical industry, providing high revenue streams over relatively long periods. They also provide a major opportunity for generic manufacturers when these drugs lose their exclusivity. With several major blockbuster drugs reaching patent expiry, the market for generic pharmaceuticals in the United States is booming and is set to witness significant growth over the next few years. Over 150 products, including 20 blockbusters, with \$77 Billion in total branded drug sales in the US are coming off patent by 2012. Here is a short list of some of the major “blockbusters” that are losing their exclusivity in the US and that will fuel the generic industry. ●

2008	2009	2010	2011	2012	2013
Casodex	Alna/Flomax	Aricept	Actoos	Avandia	Detrusitol
Fosomax	Ambien CR	Cozaar	Oxycontin	Diovan	Evista
Prograf	Arimidex	Gemzar	Plavix	Lexapro	Lovenox
Risperdal	Celcept	Hyzaar	Seretide	Singulair	
Seroxat	Keppra	Lamictal	Seroquel	Viagra	
Valcote	Imigran	Levaquin	Zyprexa	Xalatan	
	Prevacid	Lipitor		Zeldox	
	Topamax	Protonix		Zometa	
	Valtrex	Taxotere			



### Opportunity Alert: Felodipine

Felodipine is a calcium channel blocker (calcium antagonist), a drug used to control hypertension (high blood pressure). Felodipine is the generic version of the AstraZeneca's patented product Plendil which came off patent in 2007. The US market size is estimated at \$275mn - \$300mn as of 2007.

Veeda has the methods developed for Felodipine and according to the FDA; there are only current 2 ANDA holders for Felodipine. ●

### Crystal City III Conference Report on assay reproducibility assessment

The Conference Report of the third AAPS/FDA Bioanalytical Workshop (1) held in May, 2006, called for incurred sample reanalysis (ISR) to be conducted for both nonclinical and clinical studies. While providing a general framework and a rationale for ISR, the Conference Report did not provide detail about how to conduct ISR or what would be considered acceptable ISR performance.

A SOP or study plan is critical to the proper conduct of ISR assessments. The SOP or plan should detail the method of conducting ISR, how differences between original and reanalyzed results are computed, what acceptance criteria will be used, how an investigation of a failed ISR assessment will be conducted, documented, reported, and archived, and where assessment results will be reported and archived. ISR Assessment Timing and Scope ISR assessments should be conducted.

Sample size considerations are critical, and the number of samples repeated for ISR should be representative of the study conduct in its entirety and method performance overall. To eliminate confusion and facilitate a straightforward process for conducting ISR and, based on discussions since the Workshop, a sample scheme that uses a fixed percentage of the total sample size is recommended. While there are other proposed methods for calculating the number of ISR samples, the number of samples repeated should equal 5–10% of the total sample size, with 5% as the minimum for larger studies.

If you are interested in reading the entire Crystal City III Conference Report on assay reproducibility assessment, please send Vince Scamacca an email at [vincent.scamacca@veedacr.com](mailto:vincent.scamacca@veedacr.com) so that he can send you a copy of this report via email. ●

### Highly Variable Drugs

It is widely believed that acceptable bioequivalence studies of drugs with high within-subject pharmacokinetic variability must enroll higher numbers of subjects than studies of drugs with lower variability. In 2003–2005, the OGD reviewed 1,010 acceptable bioequivalence studies of 180 different drugs, of which 31% (57/180) were highly variable.

Of these highly variable drugs, 51%, 10%, and 39% were either consistently, borderline, or inconsistently highly variable, respectively. It was observed that most of the consistent and borderline highly variable drugs underwent extensive first pass metabolism. Drug product dissolution variability was high for about half of the inconsistently highly variable drugs. They could not identify factors causing variability for the other half. Studies of highly variable drugs generally used more subjects than studies of lower variability drugs.

It was concluded that about 60% of the highly variable drugs we surveyed were highly variable due to drug substance pharmacokinetic characteristics. For about 20% of the highly variable drugs, it appeared that formulation performance contributed to the high variability. ●

### Biotech Drugs Need Only 7 Years Protection, U.S. Says

June 25 (Bloomberg) – Biologic drugs should be subject to generic competition in the U.S. after seven years, the Obama administration said, calling it a "generous compromise."

Access to cheaper copies of medicines made by [Amgen Inc.](#), [Roche Holding AG](#) and other biotechnology companies is "a key element" in reducing health-care costs, White House officials said in a letter to Representative [Henry Waxman](#) obtained today by Bloomberg News. Brand-name companies have lobbied for 12 to 14 years of exclusivity, while Waxman proposed only five.

Americans spend more than \$60 billion a year on biologic drugs to treat cancer, rheumatoid arthritis and other serious illnesses at a cost of as much as \$200,000 for each medicine, Ernst & Young estimates. Unlike conventional pills, biologics can't be copied even after patents expire. Patient groups, payers and generic drug makers have battled biotechnology companies for more than two years over how to allow competition.

"Lengthy periods of exclusivity will harm patients by diminishing innovation and unnecessarily delaying access to affordable drugs," wrote [Nancy-Ann DeParle](#), director of the Office of Health Reform, and [Peter Orszag](#), director of the Office of Management and Budget, in the letter dated yesterday.

Obama has urged lawmakers to rein in record health-care spending, expand coverage to the 46 million uninsured and modernize record-keeping. His proposed budget in February called for legislation allowing generic biologics after a period "generally consistent" with the 1984 [law](#) that provides five years of protection to most conventional pills and seven years of protection to so-called orphan drugs for rare diseases. ●



# The ANDA Pulse Summer 2009

## Access to Patient pools in India

India provides one of the largest patient pools for both infectious and chronic diseases. Similarly, India also has one of the highest numbers of patients for other chronic diseases such as cardiovascular, neurological disorders, respiratory disorders and obesity. Apart from chronic disorders, the country also provides one of the largest numbers of patients for such infectious diseases as HIV, malaria and tuberculosis.

At present in India there are about 45 million asthmatic patients, 40 million diabetic patients, 8-10 million people with HIV, 8 million epileptic patients, 3 million cancer patients, more than 2 million cardiac-related deaths, 1.5 million people with Alzheimer's disease; 15% of the population is hypertensive, and 1% suffers from schizophrenia<sup>1</sup> In order to give best treatment to above diseases research on humans is both necessary and desirable. ●

## Cancer in India

Cancer is a leading health problem in India, where there are 2 to 2.5 million cancer patients at any given time, with 700,000 to 900,000 new cases occurring each year.

With increased life expectancy, migration from rural areas to cities and lifestyle changes, diagnosis and treatment of Cancer in India has increased significantly. Tobacco-related cancers account for almost one-third of all cancers in India—predominantly head and neck, lung, and esophageal cancers.

Indian women most commonly suffer from cervical, uteri and breast cancer. The incidence of breast cancer in India is increasing with an estimated 80,000 new cases diagnosed annually. Unfortunately, Indian patients do not seek early diagnosis. More than 70% of all cancers in India are found when the disease is so advanced that treatment is much less effective. ●

## Generic Oncology Research

Oncology focused drug developers have begun to struggle with an increasingly fractured market, organ drug indications, pressure on prices, increased competition for patients in trials and generally disappointing pipeline results.

Quite a lot of companies are suddenly finding they have less than stellar compounds in phase III and a raft of agents in development in phase I plus a big hole in the middle. It's hardly surprising therefore, that many of them are searching for generic companies to buy and take up the shortfall with generic oncology drugs.

Generic drug developers have taken notice and several have started to target a portion of their development efforts to developing generic versions of Oncology products themselves. The challenge for generic companies is the lack of the highly **specialized and scientific knowledge** of how their drug treats a certain disease and **access to patients for their clinical trials**.

Oncology clinical trial enrollment can be very challenging. The number cancer patients willing to participate in clinical trials is relatively low compared to the number of cancer drugs and vaccines in development. In addition, cancer is not a single disease but many diseases, with the majority of cases classified as a rare disease. Breast cancer is not just breast cancer, it can be triple negative, Her2+, or metastatic. As cancers and drugs become more personalized, the challenge for finding and enrolling patients becomes even more daunting. Choosing the right CRO to handle their studies then becomes even more important to a Sponsor when outsourcing their generic oncology studies. ●

## We Know Oncology

Veeda Clinical Research is not only **India's largest CRO**, but we are **the only Indian CRO that has a focus on Cancer research**. Our subsidiary **Veeda Oncology** specializes in Global Oncology clinical research for the world's largest pharmaceutical companies. **We understand Oncology** and have the type of expertise you need in a CRO partner to assure your study is done right!

- **Veeda Oncology is a full-service Oncology CRO** focused on all phases of Oncology research (phase I – IV)
- Has access to more than 110 sites and 110,000 patients across the Globe
- Offers a large population of treatment naïve patients ●

**Table1: Comparison of cancer rates in India and the United States<sup>5</sup>**

	India		United States	
	Male	Female	Male	Female
Cancer Rates, all sites except skin	99.0	104.4	361.4	283.2
Oral	12.8	7.5	6.3	3.7
Oesophagus	7.6	5.1	4.9	1.4
Stomach	5.7	2.8	7.3	3.6
Lung	9.0	2.0	58.6	34.0
Colon/Rectum	4.7	3.2	40.6	30.7
Breast	-	19.1	-	91.4
Ovary	-	4.9	-	10.6
Cervix	-	30.7	-	7.8
Endometrial	-	1.7	-	15.5
Prostate	4.6	-	104.3	-
Liver	2.3	2.0	4.2	1.7
Bladder	3.2	0.7	23.4	5.4
Kidney	1.2	0.5	11.2	6.0
Melanoma of the skin	0.3	0.2	4.2	1.7

Rates are per 100,000 population



### Spotlight on the DCGI

Most Pharmaceutical companies conducting studies in India understand that the Drug Controller General of India (DCGI) as the regulatory authority in India and India's home grown equivalent of USFDA but many not know that Dr. Surinder Singh is the person who is known as the DCGI. Dr. Surinder Singh has been the Drugs Controller General of India since February 2008 and is also the Directorate General of Health Services for the Ministry of Health & Family Welfare for the Government of India.

Dr. Surinder Singh was Director In-charge of the Regional Drug Testing Lab., (Gol), Chandigarh, in 2007 and served as the Additional Director and Head of Central Drugs Laboratory (Gol) and Deputy-Director (QC), National Institute of Biologicals, NOIDA. He was the former Assistant Professor of Microbiology and the SP Medical College in Bikaner and the Senior Demonstrator at the All India Institute of Medical Sciences (AIIMS). ●

### Gujarat to get zonal office of Drug Controller of India soon

*Express India (March 13 2009):* Ahmedabad Gujarat, the growing hub of pharmaceutical companies, manufacturing of medical devices and clinical research organizations, will soon get a zonal office of the Drug Controller of India.

This will essentially mean faster registration process and project approvals for the industry. Surinder Singh, the Drug Controller General of India (DCGI) announced this at the opening session of the 'InformExIndia 2009', a three-day exhibition and network event for fine and specialty chemicals and pharmaceutical industries.

Singh also informed that 62 Drug Inspectors' posts will be added in the state to facilitate speedy clearance of applications. He added, "The government is working for implementing best regulatory mechanisms in medical, bio-medical and medical devices industry as well as for ensuring patients' safety and safe clinical research practices." Measures like maintenance of a registry of Clinical Research Organizations (CROs), listing of data related to research designs, targets, sponsors' details and mandatory registration of CROs are also in the pipeline to bring in more transparency in the field, he said.

Singh said various "Pharmaco Vigilance Centres" will be established in select medical colleges throughout the country, in consultation with the Medical Council of India, which will oversee various aspects of safety and adherence to guidelines. ●

### USFDA Sets Up Offices in India

*Express India (January 2009):* Consumers in India and US can now benefit from the enhanced safety of food, drugs and medical devices as the US Food and Drug Administration has set up its offices in India

US officials of Department of Health and Human Services, Mike Leavitt and Von Eschenbach, who were in India for the inauguration of offices in Mumbai and Delhi said, "India warrants attention because it exports a large volume of products to US and is an increasingly popular site for clinical trials." These offices are a part of the USFDA's 'Beyond the Border Initiative' to expand consumer-protection efforts beyond America.

Initially, The FDA plans to post 10 officials in the country to work closely with industries that ship food and medical products to the US and facilitate smooth flow of trade. These officials include a director, four inspectors and five senior technical experts who will cover food, medical devices and drugs respectively. This is important as India which is the largest exporter by volume of drugs and biologics to the US will have a smooth flow of trade between the two countries. ●

### Tighter Norms for Drug Clinical Trials

*Express India (Bangalore, May 9):* The country's drug regulator plans to enforce mandatory registration and audit of CROs or clinical research organizations post-June this year. Details of the clinical trials they conduct across the country are to be brought into public domain on a Web site.

The CROs will have to register their trials with the Drugs Controllerate-General of India; they were advised to register with the Indian Council of Medical Research until now, which was often not done. Dr Surinder Singh, DCGI, said here recently that CROs were mushrooming all over, with nearly 700 trials for drugs, vaccines and medical devices taking place in the country. "The issues of credibility, quality and reliability of these trials are weighing on our mind" and the measures would raise the benchmark for trials done in India, Dr Singh said. It would also improve the image of India, which, he said, was emerging in the pharmacy of the world.

The DCGI had got the USFDA to train its staff in all the four zones in auditing CROs. It next planned to introduce audit of BE or bio-equivalence tests. ●



## The ANDA Pulse

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### On the WEB

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[www.veedaoncology.com](http://www.veedaoncology.com)

**Unleashing the  
power of India!**



### Veeda Calendar of events

**GPhA Fall Technical Conference:** October 27 - 29, 2009  
Marriott Bethesda North Hotel and Conference Center  
North Bethesda, MD

**AAPS 2009:** November 8 – 12, 2009  
Los Angeles Convention Center  
Los Angeles, CA

**GPhA Annual Meeting:** February 16 - 18, 2010  
Naples, Florida

### Specializing in Early Clinical Research

Veeda Clinical Research is **an independent full service CRO** and is the world's only Anglo-Indian CRO with Phase I operations in Plymouth (UK) and Ahmedabad (India). We have **over two decades of experience** conducting phase 1 trials in healthy volunteers and in small patient groups. Our special capabilities include: **radio-labeled, elderly, glucose-clamp, DQTc and Japanese-Bridging** studies.

#### Phase 1 Facility: India

- 116 beds with **12 intensively monitored beds** at Ahmedabad
- **6 intensively monitored beds at Nadiad**, a clinical pharmacology unit dedicated to studies with patients that have **renal impairment and urological complications**
- Veeda India is experienced in handling BA/BE studies for the FDA, WHO, MHRA, ANVISA, TGA, MCC and S. Korea.

#### Phase 1 Facility: United Kingdom

- A well established phase 1 unit operational **since 1987** having conducted over 300 exploratory and phase 1 clinical trials
- 61 beds with **21 intensively monitored beds**
- Experienced in technically-complex studies with a particular **expertise in female and elderly populations**
- On-site Safety Laboratory services
- Biomarker and large molecule PK analysis

**Veeda** has been helping Sponsors (**including 5 of the world's top 10**) attain a **competitive clinical advantage** in the marketplace for several years. Drug Development Companies today face challenges with **ever increasing goals, limited resources and shorter clinical periods**.

Call **TODAY** to learn more about how **Veeda** can help with your specific clinical requirements and objectives and to discuss how **Veeda** can **reduce your costs** and **expedite your product time to market!**

We are committed to delivering results and would welcome the chance to play a role in your drug development efforts!

For additional inquiries or questions, please contact:

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