



ECRON ACUNOVA

Accelerating Pharma time-to-market, cost effectively



Asia



Europe



Americas

The 505(b)(2) Alternative: An NDA that Saves Time and Money

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- CRO desirable profile
- Why 505 (b)(2) with Ecron Acunova?



What is the 505 (b) (2) alternative?

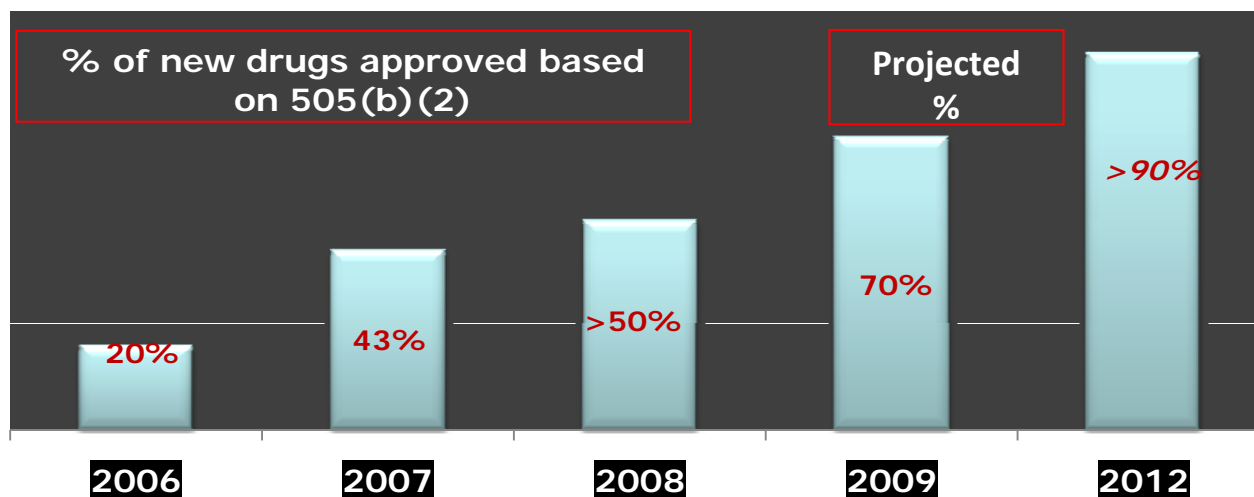
Lowers clinical development cost and time-to-market

Application type	505(b)(1) NDA	505(b)(2) NDA	505(j) ANDA
Required data from studies	Safety and Efficacy Pre-clinical & Ph I-III	<ul style="list-style-type: none">•Data from published literature with no-right-of-ref to raw data.• FDA findings for safety and efficacy of a drug	Bioequivalence
New chemical entity	Yes	Yes/No	No
New Indication	Yes	Yes	No
New formulation	Yes	Yes	No
New dosage form	Yes	Yes	No
New strength	Yes	Yes	No
Patented	Yes	Yes	No
Market exclusivity	Yes 14 yrs	Yes 3-7 yrs	Only if first generic & only against other generics

Limited change to previously approved product demonstrating safety & efficacy of change



How Popular is 505 (b)(2) alternative and why? *Innovators and generic co's are using for market exclusivity*



Source: "Understanding 505(b)(2) Approval Pathway. Q&A with Ken Phelps, President & CEO, Camargo Pharmaceutical Services. As seen in the 06/02/09 edition of Pharmaceutical Online (www.pharmaceuticalonline.com) newsletter."

Patent: 505 (b)(2) products can have Orange Book-listed patents. Enjoy 30-month stay protection against generic competitors and
Exclusivity: NCE(5yrs); New Product(3); Orphan Drug(7); Pediatric extension(6 months)
Development Budget : \$5-10M compared to \$100M+ for (b)(1) and ~1M for ANDA



505(b)(2) products approved exceeded 505(b)(1) in 2008!

Compiled by Etron Acunova Oct 2009

Established Name	Proprietary Name	Applicant	Approval
New Molecular Entities			
Bendamustine Hydrochloride	Treanda	Cephalon	20-Mar-08
Iobenguane I 123 Injection	AdreView	GE	19-Sep-08
New Esters, Salts or other Noncovalent Derivatives			
Bupropion Hydrobromide	Aplenzin	Biovail	23-Apr-08
New Formulations			
Abacavir Sulfate; Lamivudine	Abacavir Sulfate	Aurobindo	19-Dec-08
Amiodarone Hydrochloride	Nexterone	Prism	24-Dec-08
Zolpidem Tartrate	Zolpimist	Novadel	19-Dec-08
New Combinations			
Adapalene; Benzoyl Peroxide	Epiduo	Galderma	08-Dec-08
Niacin/Simvastatin	Simcor	Abbott	15-Feb-08
Sumatriptan; Naproxen Sodium	Treximet	Pozen	15-Apr-08
New Formulation and New Combination			
Methyl Salicylate & Menthol	Salonpas	Hisamitsu	20-Feb-08
Drug already marketed, but Without an Approved NDA			
Morphine Sulfate	Morphine Sulfate	Roxane	17-Mar-08
Tentative Approvals			
Docetaxel Injection	Docetaxel Injection	Hospira Inc	11-Aug-08

EA What differentiates a 505(b)(2) product?

Product Opportunities

NCE (rarely), new dosage form, dosing regimen, strength, route, indication

New active ingredient (different salt, ester, enantiomer of active moiety)

Prescription to OTC switch

New Combination Products

Generic biologics / Bio-generics

505(b)(2) NDAs are not a cakewalk, nor a windfall – they often require substantial additional innovative work

EA Regulatory issues for 505 (b)(2) product

Some of the information (clinical trials, animal studies) required for 505(b)(2) approval, FDA allows to come from studies not conducted by applicant & for which applicant has not obtained a right of reference to the raw data.

Additional information on safety and efficacy, to support proposed change on previously approved drug, determines the studies to be conducted.

Accuracy & completeness of the NDA application is key to get approval from US FDA in the first cycle review

Sound regulatory advice from clinical development partner is critical for a 505 (2)(b) product

EA 505 (b)(2) advantages and challenges

Advantages

Promotes innovation

Saves time & resources

Avoids unnecessary duplicate human testing

Greater flexibility of pricing

Exclusive marketing rights

Challenges

Due to the advantages of 505(b)(2) product, space has become intensely competitive

Time to market has to be short, with optimal clinical development time.
Patient recruitment in USA is relatively slow

Cost of development has to be less, to improve product viability.
Conducting studies in USA is relatively costly.



Acceptance of foreign data by US FDA

21 Code of Federal Regulation

312.120 - Foreign clinical studies not conducted under an IND

- FDA accepts such studies to support clinical investigations in US and/or marketing approval, provided they are well designed, well conducted, performed by qualified investigators.

314.106 - Foreign data.

- (b) An application based solely on foreign clinical data may be approved if:
- (1) Foreign data are applicable to U.S. population & U.S. medical practice
 - (2) Studies have been performed by clinical investigators of recognized competence
 - (3) The data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means.

Based on product & indication, a mix of US & foreign data offers a solution of faster clinical development of 505 (b)(2) product at lower cost

Generating quality data fast, cost effectively

Typical 505 (b)(2) clinical studies that might be needed

- One or two PK studies
- Phase II dose finding study
- Confirmatory Phase III study

Applicability to US Patient population

- Caucasian
- African American
- Hispanic

Geography for quality data with speed and cost effectiveness

- Central & Eastern Europe
- Latin America
- India

FDA requirement for data quality

- CAP certified central lab
- 21 CFR part 11 compliance & computer system validation
- FDA inspected PK facilities for GCP and GLP compliance

EA CRO partner desirable profile for 505 (b)(2) studies

Regulatory Knowledge of

- 505 (b)(2) guidelines to support IND application
- Inclusion of foreign data
- Familiar with regulatory permission timelines

Service breadth

- Protocol development for 505 (b)(2) studies
- Clinical operation in Ph II and Ph III
- PK study conduct and analysis
- Central lab, CDM, Statistics, report writing

Geography coverage

- USA, Latin America
- Central & Eastern Europe
- India

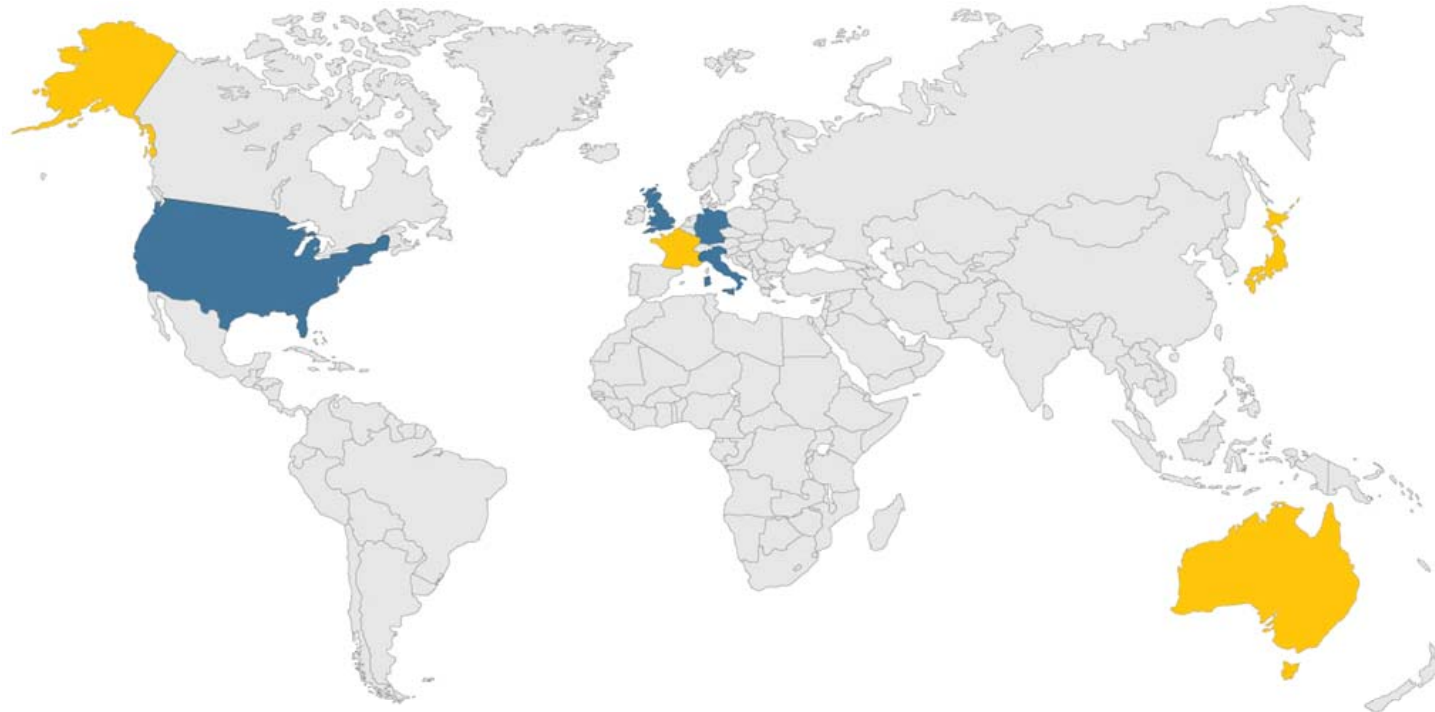
Quality and experience track record

- FDA audit
- Experience in studies for innovator and generic companies.



ECRON ACUNOVA Meets regulatory guidelines

Of USFDA, EMEA, Health Canada, DCGI ...for marketing permission



Direct Presence of EA

USA	FDA
Germany	BfArM
UK	MHRA
Italy	MoH



Presence though Partners

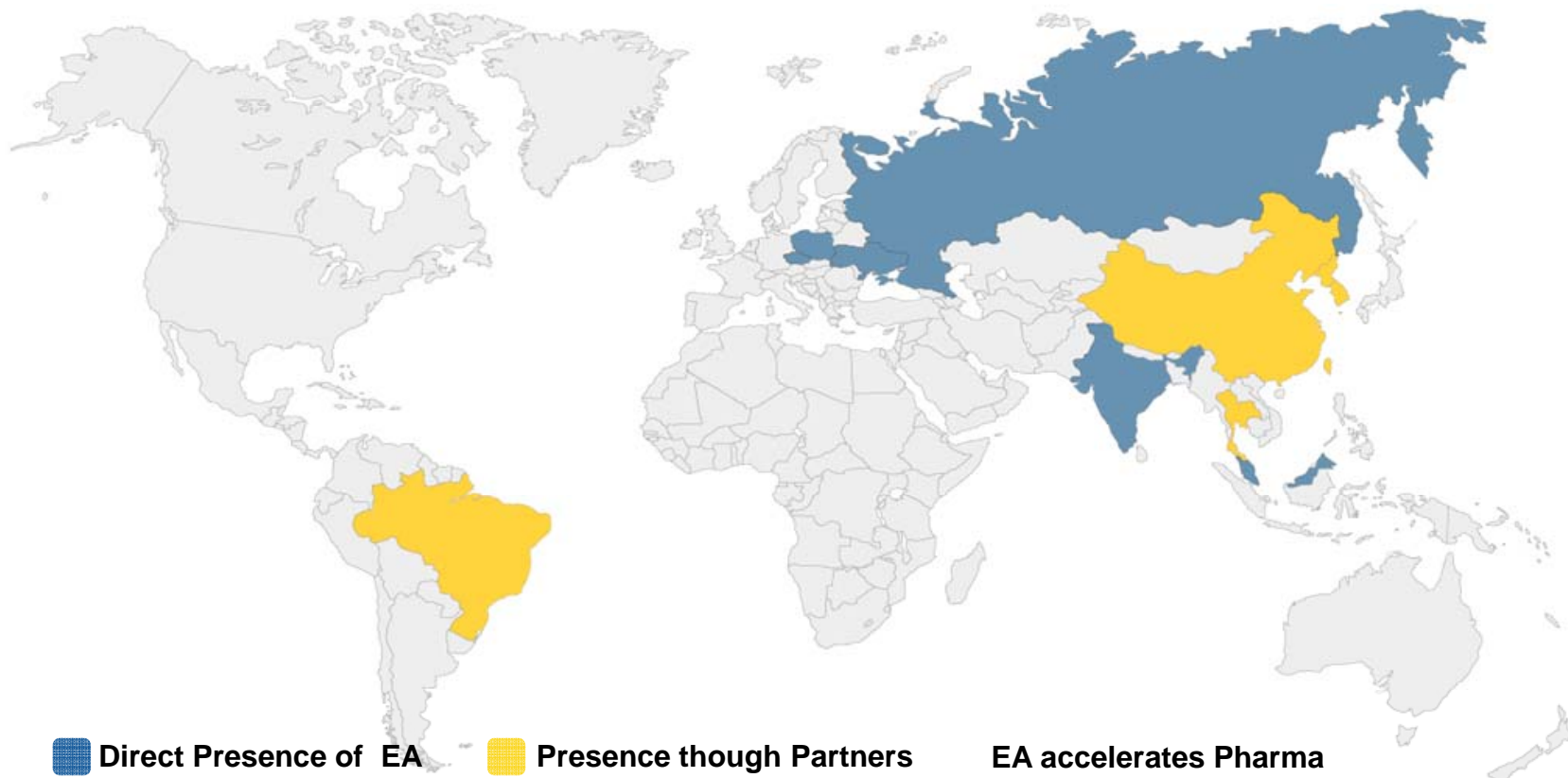
Canada	Health Canada
France	AFSSP
Japan	MHW
Australia	TGA

Studies submitted to listed regulators and sponsor got marketing approval



Speed in Patient Recruitment

Leveraging India, Central & Eastern Europe, Latin America for speed & cost



Direct Presence of EA

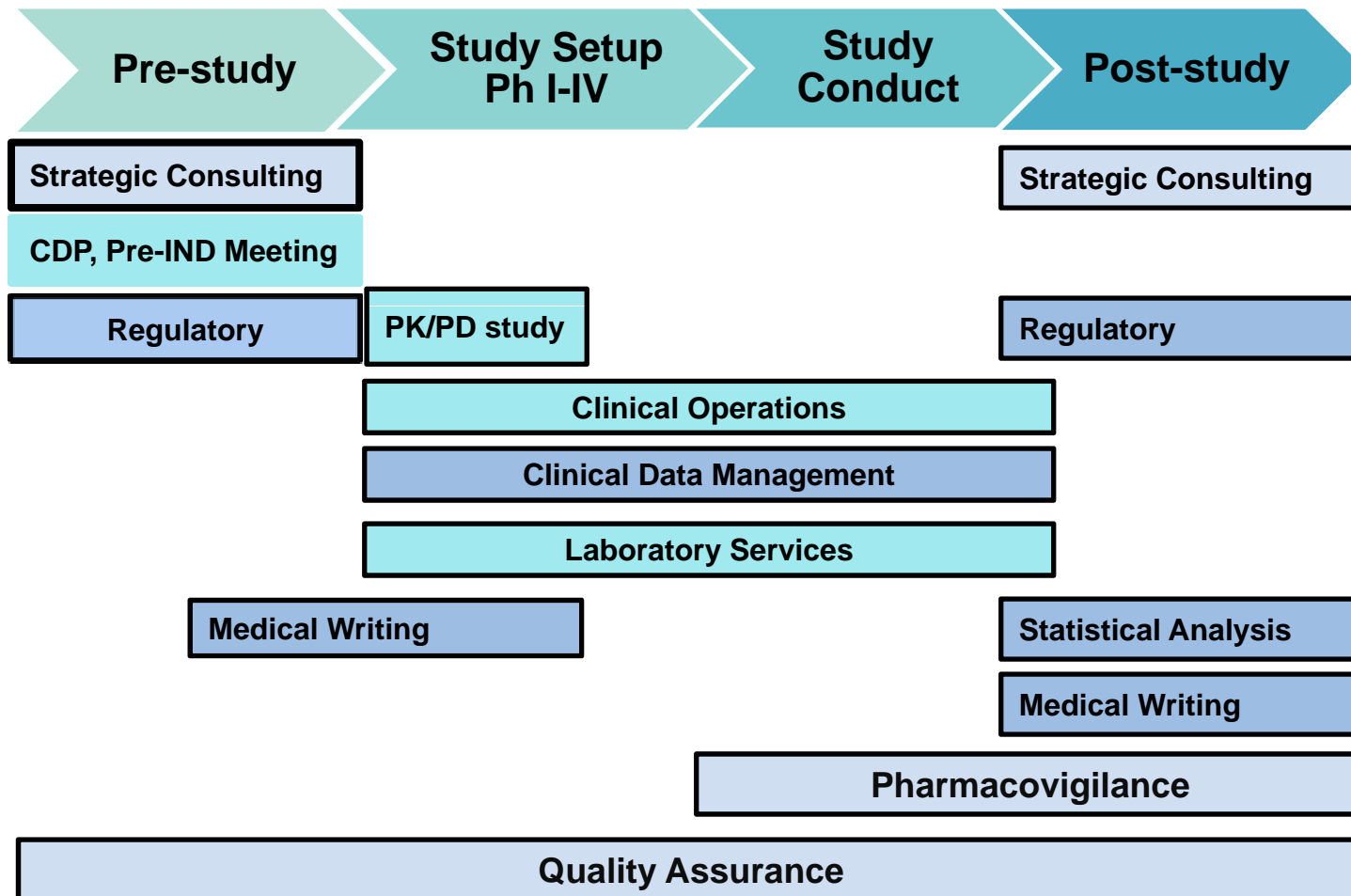
- India
- Poland & Czech Republic
- Ukraine
- Russia
- Malaysia

Presence through Partners

- China
- Brazil
- Korea
- Taiwan
- Thailand

**EA accelerates Pharma
time-to-market cost
effectively**

EA Full Service CRO with a 23 year track record





Quality Data From Studies

Studies found GCP & GLP compliant by WHO, Health Canada & US FDA




The College of American Pathologists
certifies that the laboratory named below

Manipal Acunova Limited
Central Reference Laboratory
Bangalore, India
Krathish Bopanna, DSc, PhD

LAP Number: 7195957
AU-ID: 1464874

has met all applicable standards for accreditation and is hereby fully accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to September 14, 2009 to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

Pravin Kulkarni, MD
Chair, Commission on Laboratory Accreditation

Thomas Sedman, MD FRCP
President, College of American Pathologists

UNDERWRITERS LABORATORIES INC.
CERTIFICATE OF REGISTRATION

MANIPAL ACUNOVA LTD.
Mobius Towers
SJR I Park, EPIP Zone
Whitefield, Bangalore - 560 037
INDIA

Conforms to standards for ISO 27001 based on the certificate for the first issued edition, after consulting the scope information, security management system and having it in compliance with

ISO 27001:2005

for the following scope of operations:

The Information Security Management System associated with the Design and Provision of Contract Research Services performed in accordance with Statement of Applicability (SOA) Rev: V1.0, issued 18.11.2008 of:

- Manipal Access - Europe Office at Bangalore for: Global Trials, Clinical Data Management and Central Reference Laboratory.
- Manipal Access HR Clinic of Research Centre, 4th Floor, Mobius Towers Cancer Hospital, Manipal for: Radioactivity Diagnostic Services.
- Manipal Research, 4th Floor, Arjuna Road, Bangalore for: New Management Operations.

The Information Security Management System registered is included in ICA's Directory of Registered Firms and applies to the provision of goods and/or services as specified in the scope of registration from the issuing date onwards. My acceptance of this certificate for the first registration and extension or suspension is subject to the applicable standards. This certificate is not transferable and remains the property of Underwriters Laboratories Inc. ®.

File Number: A19129
Volume: 1
Original Issued Date: October 12, 2008
ISO 27001:2005 Issue Date: October 11, 2008
Renewal Date: October 11, 2009

A. A. Bhat
John F. Schmitt
Senior Vice President, Chief Development Officer



UNDERWRITERS LABORATORIES INC.
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Manipal Acunova Limited
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EPIP Zone, Whitefield
Bangalore - 560 037
INDIA

Conforms to standards for ISO 9001 based on the certificate for the first issued edition, after consulting the scope information, quality management system and having it in compliance with

ISO 9001:2000

for the following scope of operations:

The Design and Provision of Contract Research Services in the areas of: Clinical Data, Clinical Data Management, Central Reference Laboratory and their Associated/Interconnected Studies.


The office located at Manipal performs the functions of Bio-Availability and Bio-Equivalence Studies.

Further specifications regarding the scope of the certificate and the applicability of ISO 9001:2000 requirements may be obtained by contacting the organization.

The quality system registered is included in ICA's Directory of Registered Firms and applies to the provision of goods and/or services as specified in the scope of registration from the issuing date onwards. My acceptance of this certificate for the first registration and extension or suspension is subject to the applicable standards. This certificate is not transferable and remains the property of Underwriters Laboratories Inc. ®.

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Volume: 1
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ISO 9001:2000 Issue Date: June 28, 2006
Renewal Date: June 28, 2008

A. A. Bhat
John F. Schmitt
Senior Vice President and Chief Development Officer

Audit Certificate for BVMA Audit

Auditee	ECRON ACUNOVA GmbH, Hahnstrasse 70, 60528 Frankfurt, Germany
Audit Requested By	Bundesverband Medizinischer Auftragsinstitute (BVMA) e.V., Rosenkavalierstrasse 12, 81925 München, Germany
Audit Date(s)	20-Mar-2009
Audit Focus and Scope	This audit served to assess ECRON ACUNOVA's adequacy and quality level in order to assure the BVMA that the systems, procedures, practices and documentation at the CRO comply with Good Clinical Practice (ICH GCP), relevant national and international GCP requirements, CRO policies and procedures, the Statutes of the BVMA and generally accepted good practices.
	Areas reviewed included: company overview/organization, facilities/disaster recovery, quality management, Standard Operating Procedures (SOPs), training, clinical monitoring, regulatory affairs, project management, data management, information technology, document management and archiving.
Quality Assurance Auditor	Rita Hättemer-Apostel, CEO, Verdandi AG
Audit No.	BMA003-CROAUD / 2009-AUD-40-DE-0012

Members (or applicant members) of the Bundesverband Medizinischer Auftragsinstitute e.V. (BVMA) must agree to an external, third party audit as part of the application procedure. Following the initial audit of an applicant Contract Research Organization (CRO), regular re-audits are conducted every three years to assess corrective actions implemented from the last audit (if any), compliance with current regulations and guidelines and any changes at the CRO which may have occurred since the last audit (e.g. new facilities, new services etc.). The audit program assesses the quality level of BVMA members.

Rita Hättemer-Apostel
Rita Hättemer-Apostel
CEO, Verdandi AG

2 June 2009
Date

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CSV & 21 CFR Part 11 Compliance certified by Lachman Consultants NY



Service portfolio

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SERVICES	INDIA	EU
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Regulatory		
Phase I 144 beds In India: offer First-in-Man, Phase I, BA/BE Offer service in Europe through alliance partner	171	10
Phase II-IV Full Service. Multinational in Europe Monitors speak national language	99	141
Central Lab ISO/CAP certified at Bangalore and Manipal Compatible with partner labs in USA and Europe	220	
CDM Paper and eCRF Oracle Clinical™ Biostatistics SAS™ Medical Writing	42	72

No. of studies since 2005

EA Why 505 (b)(2) with Ecron Acunova?



505 (b)(2) alternative

- Promotes innovation
- Improved safety and or efficacy
- Avoids duplicate human testing
- Saves time and cost
- Provides marketing exclusivity and patent.

Ecron Acunova

- Regulatory expertise for 505 (b)(2) study
- Full service including PK, Lab, CDM
- Present in USA, India, Central/Eastern Europe & Latin America.
- US FDA audited.

23 yrs reputation for Quality, speed & cost effective service

Accelerating Pharma 'time-to-market' cost effectively

CRO partner of choice



Contact us www.ecronacunova.com

We accelerate Pharma time-to-market cost effectively



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Thank You