



NB&A Srl Res. CERCHI,
App. 202 MILANO 2
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NB&A a full service **Clinical Research** **Organization since 1983**

NB&A is one of the oldest CROs in Italy, since 1983, first under the name "Nino Bergamini & Associati", and since 1995 under the name "NB&A" which was the company's logo during the first 12 years of activity. Over more than 20 years NB&A has performed a number of activities on behalf of numerous of Italian and International companies.

The company was founded by Dr. Nino Bergamini, MD. who is now the Scientific director of NB&A srl. Graduated in Medicine of the University of Pisa, Postgraduate in Hygiene and Public Health, at the University of Bologna, Member of the British Medical Association, and of the New York Academy of Science, Fellow Faculty of Pharmaceutical Medicine UK, he covered positions of responsibility with different pharmaceutical companies including:

Dow-Lepetit. as Associate Corporate Medical Director.

Farmitalia-Carlo Erba, as Director Therapeutic Research.

Ciba Geigy Basel, as Head Rheuma/Pain clinical Research Team.

He was Rapporteur on therapeutic research progress at the Treatment Committee of the International Congress of the Union against Tuberculosis Moscow, 1973.



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Because of his research activity in the field of infectious diseases, mainly tuberculosis, in 1981 in Prague Nino Bergamini was awarded the Medal of the Purkinje Medical Society. At the time, he was the only western MD working with the pharmaceutical industry to receive this award.

He is the author of over 60 papers mainly in the field of clinical research with antibiotics, anti tuberculosis drugs, and NSAIDs.

NB&A is composed of an experienced team of dedicated professionals that provide international clinical research and development services to the pharmaceutical industry, and information technology services.

Quality is our pride.



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NB&A in Europe

NB&A bases its country-specific know-how on the several decades of the field-activity of its collaborators.

Dr. Nino Bergamini started organising and conducting clinical research in pneumology, rheumatic diseases and hypertension in central Eastern Europe in 1967. The personal relationships built during those years have paved the way to NB&A activities in those countries of medical excellence .

NB&A has been conducting clinical research activities in almost the whole of Europe. We are in position to identify and validate clinical research centres, to care for regulatory activities, for defining financial agreements with centres/investigators and, upon request to handle the payment of study grants.

The countries in which we conducted clinical research in these years are:

Austria	Germany	Poland	France
Belgium	Hungary	Switzerland	Norway
CIS	Italy	Slovenia	the Netherlands
Croatia	Latvia	Czech Republic	the UK

We have also relationships with Japan, Ukraine, and the USA.



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NB&A Services

NB&A services span all phases of clinical trials, from conception to data management and reporting:

The conception phase

- Critical evaluation of available data
- Product study
- Conception of a product development plan
- Writing of an investigator brochure

Protocol preparation

- Phase I studies
- Bioequivalences
- Pharmacokinetics studies
- Pharmacodynamics studies
- Phase I to III studies
- CRF development and design (w. patient diaries)
- Translation of necessary documents in local languages

Regulatory process

Preparation and follow up of regulatory authorities authorizations in Croatia, Czech Republic, Italy, Latvia, Poland, Slovenia

Quality assurance

- CRF vetting, including those CRFs managed by sponsor
- Adverse Event coding (WHO-ARTdictionary)
- Query generation and resolution, including on sponsor managed studies
- Quality check on databases on all data and/or
- Quality check of a random extracted database sample
- On-site audit visits
- AE Management

Data management & statistics

- Database design, entry forms design
- Design and coding of input validation programs
- Data entry
- Statistical analysis of study data
- Tabulations and listing, tailored to the study specifications

Data management & statistics tasks can be performed on study material originated by Sponsor conducted studies

Study management

We conduct studies in Croatia, Czech Republic, Italy, Latvia, Poland, Slovenia and other countries in Europe, Japan, and the USA.



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NB&A Data Quality Assurance

Quality control data from the relevant section of a clinical study report rendered anonymous:

The accuracy, completeness, consistency and reliability of the data was assured by the following actions:

The check of the original source documents had to include: the signed informed consent; the record of the X-ray interpretation; the record of the ECG tracing interpretation; the printed records of laboratory data; the work-sheets if available where vital signs and efficacy measurements were recorded during each visit, dated and initialed by the investigator.

Sponsor's and/or CRO's personnel were allowed to review these documents at their request. Appropriate standards of confidentiality were maintained.

The clinical study monitors visited each study site at monthly intervals. Upon each visit they performed 100% CRF review versus source documents and the sponsor's representatives conducted on site audits of study generated data.

Seven on-site audits were performed at 6 centres in the Czech Republic and one in Zagreb, Croatia.

QA personnel performed in-house CRF vetting. The data entered were checked for consistency by an ad-hoc software program. Whenever needed, QA issued queries that were brought to the attention of the investigators by the CRO's CRAs and solved.



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NB&A Database Verification

An example of database verification from one of company's study report:

The complete database consisting of 777'510 data points was printed in form of data listings patient by patient and fully compared versus the relevant CRFs. This procedure allowed detection not only of possible data entry errors (that could have been identified and corrected by double key stroke data entry) but allowed to detect the few inconsistencies possibly overlooked at the centralised revision mentioned above and at the verification performed visit by visit by the study monitors. The errors were corrected and queries were issued for the inconsistencies detected and the answers to the queries were appended to the relevant CRFs, duly recorded and entered in the database.

Eventually 5% of the data present in the corrected database were randomly extracted. This resulted in a list of 38'875 data that were carefully checked against the relevant CRFs by independent quality assurance personnel. A total of 14 errors were detected on the 38'875 data points verified i. e: 0.0334%, (confidence limits 95%= 0.02 to 0.05) a through value (on both non critical and critical data) significantly lower than the 1% considered acceptable by the SOPs of the CRO and by the sponsor.



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NB&A Experience (Clients List)

In over 20 years of activity, **NB&A** provided different services to a number of Italian and international Companies:

AABBOTT Italian subsidiary
BAYER Italia S.p.A.
BIOMEDICA FOSCAMA S.p.A. Italia
BRISTOL MYERS SQUIBB S.p.A.
CHIESI Farmaceutici S.p.A Italia
CRINOS S.p.A. Italia
ELY LILLY S.p.A. Italia
EURAND Italia S.p.A.
FARMITALIA-CARLO ERBA S.p.A. Italia
HOECHST Italia S.p.A.
HOFFMANN LA ROCHE AG Basel CH.
MENARINI RICERCHE S.p.A.
PIERRE FABRE S.A.
POLICHEM S.A. Lugano CH.
RHONE POULENC SA. Paris
SCHERING S.p.A. Italia
SIEGFRIED AG Zofingen CH.
SIGMA TAU S.p.A. Italia
SMITHKLINE BEECHAM S.p.A. Italia
SQUIBB Princeton Inc.
TAKEDA Italia S.p.A.
WELCOME Italia S.p.A.
UCB SA Bruxelles
ZAMBON S.p.A. Italia



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NB&A Experience

(Examples of Field-Activity)

NB&A has matured a great experience in many fields of the Clinical/Pharmaceutical research:

Gastrointestinal

- Ulcerative colitis
- Irritable bowel disease
- Gastroduodenal ulcer

Cardiovascular

- Hypertension
- Coronary heart disease
- Vein thromboembolic disease
- Peripheral arterial disease
- Vascular skin ulcerative disease
- Stroke

Infectious diseases

Dermatology/Cosmetology

- Skin irritation/tolerability tests
- Skin sensitisation evaluation
- Sun radiation protection
- Skin elasticity
- Skin hydration
- Treatment of onychomycosis
- Wrinkle management



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Central Nervous System

Epilepsy

S DAT

Endocrine/Metabolic diseases

Diabetes

Osteoporosis

Choloproctology

Haemorrhoidal disease

Antibacterial/Antiviral Agents

Respiratory tract infections/bronchitis

Hospital acquired pneumonia

Urinary tract infections

Skin and appendages fungal infections

Treatment of infected skin lesions

Pulmonary tuberculosis

Oncology

Breast cancer

Oncohaematology

Renal cell carcinoma

Respiratory tract/Allergology

Asthma

Hay fever

Reumatology

Rheumatoid arthritis

Osteoarthritis

Minor rheumatic complaints



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NB&A Experience

(Documentation of results attained)

Most of company's attainments are documented only by confidential internal reports, study protocols and related documents, many of which, even if formally no longer covered by confidentiality agreements, would be unfair and unethical to disclose as a company's promotional tools. Some have been presented at conferences/meetings or published.

The following papers present the results of a few of the studies carried out by NB&A:

Psichiatria

Italian epidemiology study on depression.

Gastrointestinal

Phase I three way, single dose pharmacodynamic study in healthy volunteers, comparison between a novel H2 antagonist, placebo and ranitidine of the gastric secretion inhibition profile onset, peak duration (integrated clinical statistical study report to sponsor).

Phase II, III dose finding in ulcerative colitis, protocol design, CRF and study forms design, identification of centres, study conduct (integrated clinical statistical study report to sponsor).

IBS protocol design, according to the EMEA/CPMP guidance CRF and study forms design, identification of centres, study conduct (integrated clinical statistical study report to sponsor).

Haemorrhoidal disease protocol design, CRF and study forms design, centres identification, study conduct (integrated clinical statistical study report to sponsor).



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Cardiovascular

Angiology:

Planning organisation and conduct of the European double blind, randomised multicentre study, in peripheral arterial occlusive disease 24 centres in (Austria, Croatia, France, Germany, Italy, the Netherlands, Russia, Switzerland, UK), 12 months randomised treatment, 458 evaluable patients. Protocol, CRF, diary and study forms design. Design of the Q.o L. questionnaire validated as ST27 questionnaire. Monitoring quality assurance. Data management, CRFs vetting, queries. Writing of the Product Investigator Brochure.

See papers:

European Multicenter Study on Propionyl-L-Carnitine in Intermittent Claudication. Brevetti G. et al. J. Amer. College of Cardiology, 1999, 34(5):1618-24

Un nuovo questionario per la valutazione della qualità di vita nel paziente affetto da claudicatio intermittens. Silvestro A. et al. Minerva Cardioangiologica, 2000, 48:1-11

Coronary Heart disease:

Protocol and CRF design, centre identification and validation double blind randomised evaluation of the efficacy and tolerability of a Ca antagonist formulation in effort angina. 48 patients 8 centres in France, Italy and Sweden; monitoring, CRF vetting, queries, data management (integrated clinical statistical study report to sponsor).

Centre identification and validation for double blind randomised evaluation of the efficacy and tolerability of a transdermal vasodilator formulation in effort angina. 80 patients, 14 centres, monitoring CRF vetting, data management (integrated clinical statistical study report to sponsor).



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Myocardial Infarction:

Planning contribution to study protocol, centres identification and validation, monitoring, CRFs vetting, data management for a double blind randomised, multicentre study in Italy.

See paper:

The Effect of the Angiotensin-Converting-Enzyme Inhibitor Zofenopril on Mortality and Morbidity after Anterior Myocardial Infarction, Ambrosioni E., et al. New. England Journal of Medicine, 1995, 332, (January, 12):80-85.

Hypertension:

NB&A has conducted several double blind, randomised, controlled studies with ACE inhibitors, Ca antagonists, combination products, either dose finding studies or phase III comparative studies. In most cases NB&A was responsible for protocol design, CRFs and study forms, centres identification and validation, regulatory activities, monitoring, CRFs vetting, data management and final study reports. NB&A and study centres have been audited by different Sponsor's representatives. Studies have been carried out in Italy, Czech Republic, Croatia, Germany, Austria, Latvia, Poland and Slovenia.

For most studies, only integrated clinical statistical study reports to sponsor have been produced.

See the most recent abstract:

The MAISH study (Manidipine vs Amlodipine in Isolated Systolic Hypertension study in aged patients): ambulatory blood pressure results after 3 months of treatment. 2006. Paper submitted to the Congress ESH 2006, Madrid.

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Pulmonary disease

NB&A has collaborated in several studies in asthma and related diseases.

Most phase III double blind randomised studies in adults included at least collaboration to protocol development, CRF and study forms development, centres identification and validation, regulatory activities, CRFs vetting and queries, data management. In most cases only integrated clinical statistical study reports to sponsor were produced. Studies were carried out in selected centres in the Czech Republic, Croatia, Lithuania and Poland.

NB&A collaborated in the development of cetirizine in hay fever in Switzerland and in Italy.

See paper:

A placebo-controlled trial of cetirizine in seasonal allergic rhino-conjunctivitis in children aged 6 to 12 years, Masi M., et al. *Pediatric allergy and Immunology*, 1993, 4(suppl.4):47-52.

Central Nervous System

Collaboration to the protocol development and the design of CRF and study forms and to the organisation of the investigators training for homogeneity in the application of study questionnaires for European study in SDAT intended to involve France, Germany, and Italy on behalf of an international sponsor.

Planning and conduct of a study in epilepsy in adult patients.

Oncology

On-site data verification and survival data control for a study with a radio-sensitizing agent CRF vetting and coding, data management, statistics, Integrated clinical-statistical report.

Activities carried out at several centres in France (Paris, Mulhouse) and in UK (London, Cambridge).

Renal cell carcinoma study on-site survival data control.

Activities performed in France, Italy, Norway, Switzerland.



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Infectious disease

NB&A was entrusted with the responsibility for CRFs quality control vetting, coding, issuing queries, data management, statistics, report writing for the novel oral cefalosporin by Hoffman La Roche. Over 5000 CRFs coming from everywhere in the world. Argentina, Austria, Belgium, BRD, Brasil, Finland, France, Greece, Hong Kong, Singapore, etc.

NB&A produced a series of integrated study reports by study and or by centre of cumulative safety reports of reports dealing with microbiology sensitivity/resistance patterns. Only such internal integrated clinical statistical study report to sponsor were produced.

Similarly NB&A was entrusted with quality assurance, data management, statistics and medical writing for a number of phase IV studies with an injectable cefalosporin.

NB&A has collaborated to the Italian arm of two international studies in hospital acquired pneumonia.

Dermatology:

Controlled study in the topical treatment of infected skin wounds at general practitioners' sites in France. Protocol, CRF development, data vetting, data management (integrated clinical statistical study report to sponsor).

European multicentre, multinational long term randomised, study of the efficacy of a new lacquer versus its own placebo, (double-blind) and a standard reference, (single-blind) with final evaluation by a blinded independent observer. 16 months of observation, 476 randomised patients, over 20 centres in 6 countries (Czech Republic, France, Germany, Italy, Latvia, Poland), NB&A was responsible for protocol development CRF, diary and study forms design, regulatory activities, monitoring, CRF vetting and coding, data management, statistics and integrated clinical statistical report.