CURRICULUM VITAE

Manuela Brugnolotti
Art in Science di Manuela Brugnolotti
Consulting Services for Bio & Pharma

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PROFESSIONAL CURRICULUM

Consultant (Art in Science)

Aug. 07 - Present

Currently I am working as an independent consultant on my own (Art in Science, being the managing director) or co-operating with other consultant companies (e.g. PharmaCentaur AG).

The consultant work regards the following main topics:

Tech-Transfer activities:
For transfer of manufacturing process: Preparation of Project Plan, Transfer Master Plan, Risk assessment, Sampling plan and Process flow chart, preparation of campaign reports for the produced products evaluating the results, preparation of process validation protocols and reports;
For transfer of analytical methods: Preparation of Project Plan, Preparation of Analytical Methods transfer plan (AMTP), including risk assessment, Preparation of Analytical Methods Transfer Report (AMTR).
Quality Assurance activities: critical analysis of quality documentation such as validation protocols, validation reports, SOPs, risk assessment, sampling plan, etc.; tech-transfer projects, including gap analysis, preparation of documents, evaluation of documents, preparation of corrective actions; FDA-readiness projects; training on GMP guidelines; implementation and management of quality integration projects on various sites; preparation of best practices/standards, gap analysis and preparation of remediation corrective actions; preparation of presentations for inspections (FDA, EMA, etc.);
Project management: co-ordination of global international team for preparation of best practices and standards; co-ordination of quality integration projects for validation, stability and environmental monitoring; gap analysis, remediation activities, tech-transfer, documents management, etc.;
Production/QC activities: input regarding preparation of production documents and SOPs, preparation of best practices/standards, position papers, and sampling plan; review of BR; gap analysis, preparation of remediation corrective actions; work organization; managing of QC stability group; perform audits for stability and other topics; preparation of stability protocols and reports;
Regulatory Activities: preparation of regulatory strategies for developments projects and marketed products; preparation of the CMC documentation for regulatory submissions such as licence applications, variations, annual report, renewals, IMPD, IND etc; preparation of documentation for meetings with main Health Authorities (EMEA/EMA, FDA, European National Authorities, TGA, etc.); provide regulatory review to regulatory documents; liaise with other departments in the company in order to obtain all the necessary information required for regulatory submissions; liaise with other third party manufacturers and/or suppliers in order to get all relevant information/documentation for regulatory submissions; provision of regulatory advice and guidance to other departments (e.g. Quality Assurance, Production, Quality Controls, etc) and to quality/production documents; interpret and anticipate implications of new guidelines; troubleshooting and problems solving; set-up of regulatory organization/department; regulatory training for junior positions;
Due diligence: for the acquisition of products and companies;

I have worked for Novartis Vaccines and Diagnostics on global quality integration projects (as project leader and project manager, I had also performed audits on sites, and participated to QALT (Quality Leadership Team) weekly meetings), and on local projects (helping the Italian site in the preparation of stability documents, type C meeting, presentations for inspections, meetings with Health Authorities, including FDA,

and managing the stability group for more than one year with 2 successful PAIs in one month). I have also performed gap assessments on the documentation for a product to be submitted in EU/US, produced at different sites.

For Sandoz, I managed five tech transfers from Development site (Central Europe) to the production sites (Central and Eastern Europe, Switzerland and India), including managing the production of clinical batches for EU and US. This assignment include the preparation of documents such as transfer production reports, manufacturing reports, risk assessment, sampling plan, transfer master plan, process flow chart, process validation protocols and reports, etc..

I have also worked for other pharmaceutical companies that do not want to be mentioned for confidential reasons, for regulatory activities and tech-transfer topics, both for manufacturing and analytical transfer.
I have performed due diligence for the acquisition of products, assessing the available documentation, competitors' products and providing regulatory advice.

Regulatory Pharmaceutical Industry Experience

April 2006 – July 2007
Novartis Vaccines & Diagnostics, Siena.
RA Head of Flu & Respiratory Franchise
Novartis acquired Chiron in April 2006 and created the new division Vaccines & Diagnostics. In the new organization I had the same role I had in Chiron Vaccines and then I was assigned special projects for the registration of flu vaccines in the US. In addition I have participated in some tech-transfer projects for transfer of filling operations (sterile product filled in syringes) from Italy to Spain; transfer of production of antigens from Italy to the UK; transfer of final bulk (sterile product) from Italy to Spain.

Apr. 99 – April 2006
Chiron Vaccines, Siena.
Regulatory Affairs Manager (Apr 1999 – Dec 2003)
RA Head of Flu & Respiratory Franchise (Jan 2004 – Apr 2006)
From 1999 until 2001 I was responsible for the Siena flu products for Europe and Eastern Europe. In this period I submitted several variations for a product already approved with a MRP, and a parallel double MRP for another flu product.
My role included communication with all the Health Authorities in Europe and the RMS (Italy for this procedure) and the partners involved, planning of new registrations with Commercial Operations, planning of new variations/procedures with production/QC/QA/clinical personnel. I also participated to EVM (European Vaccine Manufacturer) Regulatory Working Group on behalf of Chiron Vaccines. At that time I was also responsible for two development projects: the pandemic project and the intra-nasal flu project. Three people reported to me and I reported to the Head of RA of Siena and Marburg (Germany) Sites.
From January 2002 to December 2003 I was given the responsibility worldwide for these products (nearly 80 countries around the world, including Australia, China, South Korea, Singapore, etc.) the responsibility for other two Italian copy products (registered by a sister company), the responsibility of the group based in Marburg for another flu vaccine already registered through a MRP. My role was to plan activities, define regulatory strategy, budget, co-ordinate with other functions, revise application, etc.
After the acquisition of PowderJect by Chiron Vaccines, I participated to the remediation activities for the problems occurred at Liverpool site (suspension of the manufacturing license), managing the preparation of the necessary documents to re-register the product in the UK and the variation documents for FDA for the changes introduced in the manufacturing process.
In 2005 I was appointed RA Head of Flu Franchise. A Regulatory Affairs Franchise is a virtual department spanning across sites, having the objectives of defining the strategy and implementing the RA activities related to products/projects belonging to the same therapeutic areas. A franchise is created whenever the portfolio of the Company requires the coordination of strategies and activities for products/projects that are closely interconnected. The role is to identify and develop synergies among franchise projects and to ensure compliance /alignment with the approved budget; to ensure that the company objectives are met and the agreed activities are carried out; to prioritise activities to obtain the highest quality in the shortest possible time; to

define the RA objectives related to the Franchise products/projects, in close cooperation with relevant stakeholders. In this position I reported to the Global Head of Regulatory Affairs.
The Flu Franchise included responsibility for 8 flu vaccines on the market, several projects under development worldwide and participation to Disease Area Planning, that was a committee in charge to prepare the strategy for the short (1-5 years), medium (5-10 years) and long (10-15 years) term within a franchise.
In these roles in Chiron Vaccines, I have been involved in organizing and managing meetings with various Health Authorities in Europe and outside Europe, including; EMEA, FDA, Health Canada etc. In addition I also had several meetings with potential partners in different geographical areas including; Japan, Australia etc. My responsibilities included also due diligence for possible acquisition and tech-transfer projects.
25 people reported to me in 4 sites: Siena (Italy), Marburg (Germany), Liverpool (UK) and Philadelphia (USA). The role also encompassed a regulatory compliance remit within the overall company quality system and GxP, and assistance with technical/medical enquiries. I was also directly responsible for some of the projects. Several projects/products were cross-sites. In this case my role was to assure alignment with company's goals and timelines, respecting budget.

Jan. 98-Apr. 99
Helsinn HealthCare S.A., Lugano, Switzerland.
Regulatory Affairs Manager-
I was responsible for the preparation of the registration dossiers for new and variation applications for the two-affiliate companies (in Portugal and Ireland) and for the licensors. I was also responsible for the update of two in-licensed products, in order to apply for new registrations. In addition, I was also responsible for the optical archive of the existing documentation for all the products. In this position I had one person reporting to me.

Oct. 95 – Dec. 97
Pharmacia & Upjohn, Milan
Area Manager for Eastern Europe
After the merger, I was appointed Area Manager for Eastern Europe (with a portfolio of 200 products). I had direct contact with countries of my area (including the Health Authorities), the Areas Managers, the Marketing people and the Business Areas. I prepared files for the countries, (creating abridged dossiers where appropriate) and was responsible for preparing the packaging material according to the local rules.
I was the project leader for the I.T. activities within the MC International; for the projects regarding the optical archive of dossiers, correspondence, documents sent to the countries, local requirements and EC guidelines and directives.
I was also responsible for the project regarding the dispatch of the files on CD, International database. In this position two people reported to me.

Feb. 94 – Sept 95
Pharmacia, MC International, Milan
Responsible for the Regulatory Affairs (ad interim) until Apr 95 - then Regulatory Affairs Area Manager (from May 95)
I started as Regulatory Affairs Officer in Market Company (MC) International in Pharmacia (Milan), dealing with the registration of all the Pharmacia products (with a portfolio of approximately 100 products) in Eastern Europe, C.I.S., Mediterranean Area, Middle East, Africa and Pakistan). After two months I was appointed ad interim responsible for the Regulatory Affairs in the MC International (reporting directly to the President of the MC) for all Pharmacia products. My role included set-up of the office and implementation of a system for interaction with external offices. In addition I brought a line of products back into regulatory compliance after a number of years of neglect.
I organized the I.T. for the Regulatory Affairs and then for the M.C International (installation of computers, software, networks). I was the project leader for the optical archive and the MC International database.
In May 95 I was appointed as Regulatory Affairs Area Manager for Pharmacia products for Mediterranean Area, Eastern Europe, Turkey and Iran. I reported directly to the President of the MC International. In these roles I had one direct report.

May 93 - Jan. 94
SmithKline Beecham, Milan

Regulatory Affairs Officer
My responsibilities included:
Worldwide responsibility for the registration of Elcatonin (non-natural calcitonin);
Electronic Submissions: I was the interface with the Italian Health Authorities during the first electronic submission in Italy for Fanciclovir
Responsible for products in the Inflammation and Tissue Repair Therapeutic Area, and ad interim for the products of the Vaccines Area;
Responsible for the I.T. projects within Regulatory Affairs (optical archive, regulatory database). I had one person reporting to me.

Non-Regulatory Pharmaceutical Industry Experience

Oct. 88 - Apr. 93
SmithKline Beecham (previously ISF), Milan
Researcher in the Peptide Chemistry Department at ISF, Milan (then SmithKline Beecham), working on planning, synthesis and purification of non-natural aminoacids, calcitonin analogues, fragments of N-procalcitonin and its derivatives, enzymatic hydrolysis of polypeptide (e.g. IGF-I and IGF-II). I was also responsible for the bibliographic updates within the Bone Diseases Area. I had two people reporting to me.

Jan. 87 - Oct. 88
Farmitalia Carlo Erba, Milan
Assistant to the Head of the Peptide Synthesis Laboratory and the Peptide Development and Pilot Unit in Farmitalia Carlo Erba (Milan). I worked on liquid and solid phase synthesis of several different classic and modified peptides (Bombesin antagonists, Endothelins), their chromatographic purification (counter current distribution, analytical and preparative HPLC), synthesis of intermediate for peptide production, creation of programs in Basic and DBIII to manage the data. I had two people reporting to me.

Post Graduate/Pre-Industry Experience

Jan. 86 - Dec. 86
University of Milan
Winner of a postgraduate scholarship at the Organic Chemistry Department (University of Milan) working on "new methodologies to synthetize potential biological active compounds, with reference to phosphonous aminoacids and peptides including non-natural aminoacids".

Oct. 85 - Dec. 85
University of Pavia
Volunteer at the Organic Chemistry Department (University of Pavia) working on cycloaddition catalyzed by protic and Lewis's acids.

Educational and Academic Qualifications:

III National School of Photochemistry	1982
Degree in Pure and Applied Chemistry at Pavia University (110/110)	1985
Government qualification enabling to practice as a Chemist	1986
Course to program in Basic	1987
VIII Advanced Course in Pharmaceutical Chemistry and Pharmaceutical Biotechnologies at the University of Padua	1988
CAS-ON LINE Workshop for the on line bibliographic research	1988
Government qualification enabling to use toxic gases	1989

LANGUAGES:
Mother language: Italian; Fluent in written and spoken English;
Basic understanding of written French.

I.T. KNOWLEDGE:
Good knowledge of the main systems and software: DOS, Windows, Office automation (Word, Excel, Power Point, Access, Microsoft Project, Visio).

COURSES AND SYMPOSIUMS ATTENDED:

4th Novartis Global Stability Conference, Siena, June 10-11, 2010 **speaker** with a presentation on "temperature excursion approach: a case study"	2010
Novartis Vaccines and Diagnostics: Validation best practice workshop, Marburg, May 13-15 2008, **speaker** with a presentation on "Review of validation gap database"	2008
12th International Congress on Infectious Diseases (ICID), Lisbon, June 15-18, 2006	2006
Second European Influenza Congress (ESWI), Malta, September 11-14, 2005	2005
I benefici della vaccinazione influenzale (Advantages of influenza vaccination), Perugia (Italy), June 22, 2005	2005
DNA Vaccines Forum, London, March 17-18, 2005	2005
Microbial Fermentation & Mammalian Cell culture, London, July 8-9, 2004	2004
Developing International Teams, London, March 30-31, 2004	2004
Workshop on Human Pandemic Influenza Vaccine, European Commission (DG Enterprise), Brussels, November 6, 2003	2003
Meeting with PEI to discuss the pandemic preparedness, Frankfurt, September 19, 2003	2003
Meeting with EMEA (VEG) to discuss the pandemic preparedness, London, September 11, 2003	2003
Regulatory Review & CTD: How to keep flexibility in the co-marketing of Pharmaceutical products in the new regulatory framework, **speaker**, Stresa, March 19-20, 2003	2003
The First European Influenza Conference, Malta, October 20-23, 2002	2002
Understanding US-FDA Drug Submission Procedures, London, January 28-29, 2002	2002
Preparedness planning in the Community: Influenza and Other Health Threats (European Commission), Brussels, November 27, 2001	2001
Nasal Drug Delivery, London, March 26-27, 2001	2001
Understanding Drug Submissions Procedures in Japan to achieve faster Approval, London, March 1-2, 2001	2001
Adapting Successfully to Regulatory Changes in Japan, London, December 7, 2000	2000
World Congress on Options for the Control of Influenza IV, Crete September 23-28, 2000	2000

Central and Eastern Europe – Regulatory challenges in the pharmaceutical Market, Prague December 1-2, 1998 1998

Filing variations in Europe, London November 10-11, 1998 1998

The role of Pharmacoeconomics in Pharmaceutical R&D Decision Making, London, October 13-15, 1998 1998

Regulatory challenges for Pharmaceuticals in Europe, Rome November 10-11, 1997, **Chairman and speaker** "Czech Republic, Hungary, Poland and the rest of Eastern Europe. The point of view of a multinational manufacturer" 1997

Meeting between EMEA and PEFRAS held in London at EMEA office 1996

The market for pharmaceuticals and for medical equipment in Romania, Bucharest March 25-26, 1996 1996

Member states and EMEA: partnership, synergies, tools for the single market of drugs - Ideas and proposals, Rome February 27, 1996 1996

International Symposium "Regulatory Europe towards 2000", Pavia 30 May 1995 1995

20th Seminar "Evaluation criteria of registration dossier. Reference systems of European agencies", Milan, 28 June 1994 1994

Seminar on the critical aspects of International core dossier generation. Why, what, when and how. Part II - Toxicopharmacology. European School for Regulatory Sciences, Rome, Oct. 4-8, 1993 1993

Seminar on the critical aspects of International core dossier generation. Why, what, when and how. Part I - Chemistry and Pharmacy. European School for Regulatory Sciences, Rome, Sep. 20-24, 1993 1993

Pharmaceutical products and cosmetics: registration, production, labelling, advertisement, free circulation in the single market of drugs, fiscal aspects with reference to congress and sponsor 1993

SmithKline Beecham course to prepare and use the dossier for Electronic Submission, UK, August 1993 1993

VIIth International Symposium on preparative Chromatography, PREP-90, April 8-11, 1990, Gent (Belgium) 1990

TIME Manager Course 1990

PUBLISHED PAPERS:

Ginanneschi L, Bardelli F, Becherucci C, **Brugnolotti M**, Battisti E, Mattii D, Comparative studies of the purity of Agrippal® with four other influenza vaccines, poster to IVW Congress, Vienna, Austria, 18–20 October 2006

M. Brugnolotti: "Czech Republic, Hungary, Poland and the rest of Eastern Europe. The point of view of a multinational manufacturer", SiarNews 24 (3°), 19-24, 1998.

R. de Castiglione, L. Gozzini, **M. Brugnolotti**, R. Mena, M. Ciomei, I. Molinari, P.M. Comoglio and G. Gaudino: "*Bombesin antagonist*", **Il Farmaco**, 45, 1251-1263, 1990.

R. de Castiglione, L. Gozzini, M. Galantino, **M. Brugnolotti**, M. Ciomei and I. Molinari: "*Irreversible ligands for bombesin receptor*" in **Peptides**, J.E. Rivier and G.R. Marshall ed. s, ESCOM, Leiden (the Nederlands), 1990, 168-170.

R. de Castiglione, L. Gozzini, M. Galantino, **M. Brugnolotti**, M. Ciomei and I. Molinari: "*Irreversible ligands for Bombesin receptor*", accepted poster to the **XIth American Peptide Symposium**, July 9-14, 1989, San Diego, California.

R. de Castiglione, L. Gozzini, **M. Brugnolotti**, R. Mena, M. Ciomei, I. Molinari, P. Comoglio and D. Parolaro: "*Bombesin receptor antagonist*" accepted poster to the **XXth European Peptide Symposium**, September 4-9, 1988, Tubingen (FRG)

M. Brugnolotti, A. Corsico Coda, G, Desimoni, G. Faita, A. Gamba Invernizzi, P.P. Righetti and G. Tacconi: "*Diels Alder versus heterodiene in the reaction between 4-arylidene-5-pyrazolones and 2,3-dimethylbutadiene: the effect of acid catalysis*", **Tetrahedron**, 44, 5229-5242, 1988.

PATENTS:

R. de Castiglione, L. Gozzini, M. Galantino, **M. Brugnolotti**, M. Ciomei and I. Molinari: "*Bombesin alkylating analogs*", Eur. Pat. Appl. 00842 (19.7.89)

R. de Castiglione, M. Galantino, M. **Brugnolotti**, L. Gozzini, M. Ciomei and I. Molinari: "*Irreversible peptide ligands for bombesin receptor*", UK 8906 900.9 (28.3.89)

R. de Castiglione, L. Gozzini, **M. Brugnolotti**, R. Mena, M. Ciomei and I. Molinari: "*Peptide ligands for bombesin receptor: bombesin antagonist (I)*", UK 8808768,9 (14.4.88)

M. Pinza, C. Farina, **M. Brugnolotti** and R. Mena: "*Cyclic calcitonin derivatives*", UK patent appl. No. WO 93/15106 published on 5.8.93