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Biotika®: ISIFC's Virtual Company or Biomedical pre Incubation Accelerated Process

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1. Introduction

This chapter concerns a new concept of innovation in healthcare technology. ISIFC is the internal engineering school of University of Besançon (France) and is accredited by the French Ministry of National Education. The « Institut supérieur d'ingénieurs de Franche-Comté » (ISIFC) graduates 216 biomedical engineering students since 2004 for the prevention, diagnosis and treatment of disease, for patient rehabilitation and for improving health. Its originality lies in its innovative course of studies, which trains engineers in the scientific and medical fields to get both competencies. The Institute therefore collaborates with the University Hospital Centre of Besançon (CHU), biomedical companies and National Research Centres (CNRS and INSERM). The teaching team consists mainly in lecturer-researchers and researchers as well as biomedical and health industry professionals. It's an innovative engineering French school, which tries to understand the expectation of the specific healthcare and medical devices markets. It trains engineers in 3 years (2400 hours per student) with a double culture, medical and technical, who will work for 80% in biomedical industry, 10% in healthcare centre and 5% in research laboratory. They master all the life cycle of a medical device from the idea to the launch of the market. They can lead to improve product functionality, usability, safety and quality. We prepare our students to:

- Medical and biological instrumentation in general, with a special interest for Microsystems. The course's main targets are design enhancement and the development of equipment for clinical, medical and biological investigation (biochips, automated devices for biological analysis, probes, endoscopes, artificial organs and systems for physiological assistance etc…).
- The analysis, design and development of biomechanical systems. They thus receive special training on mechanical design, manufacturing engineering, and special training on materials used in surgery (metal, polymer, ceramic, composite…) as well as their different use in biological environments, ie tissues and human organs (biocompatibility). The main applications are orthopaedics (prosthesis and orthesis).

Our students play a significant role in emergence of combination products (e.g. biologic and device or drug and device).

1.1 11 months' work experience

Training periods and projects in laboratories, in health services or in companies enable ISIFC trainees to acquire practical experience, and to communicate with all the actors of the biomedical sector.

During the second year, all the students are invited to have a 6 weeks work experience (February and March) at the hospital. It enables future engineers to fully grasp the integration of biomedical equipments within a health service, from a technical and human point of view.

During their third year (master degree), students are challenged through a development project. It lasts 3 months (December to February), and the project is addressed individually. Projects may be done at a private company or at a public research department.

A working period in a company premises concludes the 3-year course. It lasts from 16 weeks up to 24 weeks (March to September). Industrial trainee engineers take on missions that are usually assigned to junior engineers within a firm.

The ISIFC engineers' specificities are their good knowledge in regulatory affairs and in the quality aspects of the technologies of health, their analysis of benefits/risks for the patient and the pre clinical investigations they can manage. In it is added strategies of tradition from Franche-Comté as mechanical/biomechanical, medical instrumentation and microtechniques.

ISIFC engineers master regulatory and clinical affairs. At the end of the training, they are able to elaborate the technical file indispensable for the CE mark and FDA and so for the launch of the European and American market. They can design and create medical devices.

In fact, ISIFC School is an important partner for medical device technology development and evaluation process. ISIFC is also a tool of effectively surveying prospective device users. These users are healthcare professionals, patients, elderly people or people with disabilities, researchers and industrials.

1.2 Why Biotika®?

To stimulate greater academia/business interactions, in 2006, ISIFC created Biotika®, a virtual company (without legal status) specialized in design engineering of innovative medical devices. ISIFC created an environment for innovation in healthcare to stimulate commercialization of new medical device, to reduce costs and to deliver faster. Marketing, regulatory and clinical affairs, service support, accounting and inventory are concerned (no manufacturing and no production engineering). This company was built on the basis of a training module at the end of 2nd year (75 hours per student) and in the beginning of the third and last year (100 hours per student). It's not only an educational entrepreneurship exercise to encourage students during their university programme. The purpose is to make discover to the pupils engineers the various facets of their future job with a real professional overview and to establish real new innovative businesses enhancing the research academic researchers or supporting real start up activities. Biotika® is guaranteeing quality throughout its organization and is systemising quality within the organization (according ISO 13 485). The idea is to sensibilize the students to the innovation, the entrepreneurship, the quality approach, and the project management with specific angles to the regulatory affairs, clinical investigations, the financing of the innovation, the industrial and intellectual properties and the market studies.

The goal of this chapter is to show how was built inside ISIFC a "catalyst" and performing tool for the innovation and the partnership research. Biotika® is in fact a cell of pre incubation of technological projects for the health, stimulating proof of concept and development of new ideas arising from patients, physicians, surgeons, universities and industrials.
An experience feedback of 5 years will be described. The virtual company works on development projects and transfers of medical devices, and is in fact real cell pre incubation. The chapter describes its collaboration in the creation of start up Cisteo MEDICAL (incubator Franche-Comté**).** It gives three examples, financial supported by OSEO and Besançon University valorisation maturing process. Different applications domains are concerned: maxillofacial surgery, dental surgery, oncology, palliative care, gastroenterology and cardiovascular diagnosis. Very recently, Biotika® obtains financial support from the French Agency of Research (ANR program Emergence) with innovative saliva substitute technique for maxillofacial surgery.

2. General Biotika® principle

The nature of this innovative concept is based on the originality of the ISIFC School. It's the heart of an innovative process to accelerate device deployment in the market. It's required strong interactions among academia, life sciences, technology, engineering and industry.
The pupils-engineers recruited in Biotika® (about 20 a year) work one-two days a week on real projects and according ISO13485 standard. Three permanent members pilot the virtual company. They are punctually assisted by university experts, secretary finance and by a technician in electronics. The CEO of Biotika® is guiding in reality ISIFC and is also associate professor in optoelectronics. The Human Resources manager is in fact an associate professor in electronics and educational responsible of this training unit. The QA and regulatory affairs manager is a half time teacher but also Quality manager in a biomedical industry Statice Santé, ISIFC partner. The director of CIC-IT (Clinical Investigation Center-Innovation Technology) of Besançon Hospital collaborates regularly with Biotika®.
Every year, a new project is developed. The students participate with the staff to the choice of the new maturation. This general brainstorming (4 hours) is just after their six weeks hospital internship.
Different scenarios are possible:

- development of a medical device new to the market
- major upgrade of an existing medical device after a regulatory affairs modifications or after device deployment in the market and first users feedbacks
- re-design of a device prototype and regulatory affairs optimisations.

3. Biotika® partnership arrangement and network

Biotika®, pre-incubation cell of technology projects for the health of the ISIFC is in fact a tool catalyst for innovation and research partnerships. All of partners are important and we have a complementary network. They need to interact with and to learn from each other.
The three permanent members of the ISIFC Biotika® (CEO, Director human resources and Director Quality / Regulatory Affairs) are full time university assistant professor. The director of the Besançon CIC IT, physician of CHU, participates regularly for validation and clinical trials.
The three categories of general customers are: patients, healthcare professionals (nurses, biomedical hospital engineers, physicians and clinical researchers) and industrials.

Four categories of customers have significant influence in the decision to innovate in the company. Firstly there are ISIFC students. The second category is prescribers (physicians, manage care organization and hospitals). The third category consists of the payers and policy makers. The last but not least category is the Biotika® permanent staff (teacher and researcher).

Biomedical engineering students recruited Biotika® work every year on real projects, detected during hospital internship and serving clinicians and patients. It's in close collaboration with research laboratories of the UFC and businesses Franc-Comtois.

Due to ISIFC links to established research laboratories in the field of engineering, micro-technologies or health (about 30 laboratories and research centres are worldwide known and associated to National Research Centres such as CNRS and INSERM), each student benefits from the most recent scientific and technological innovation and has access to up to date equipment available in these units. We work particularly with the scientific group specialized in engineering and innovative method for health (GIS) [FEMTO-ST 6174 CNRS Institute (with the French label Carnot "ability to conduct research with industrial partners), IFR 133 INSERM institute and LIFC informatics research laboratory].

The University of Franche-Comté established a Valorisation Administration in 1997 in order to develop in the institution a culture of partnership with the socio-economic environment, and to support laboratories in the valorisation process of their research results. To support this move, a SAIC (Department of Industrial and Commercial Activity), which is a valorisation management tool, was set up in 2004. An annual maturation process, called "Maturation Franche – Comté" was set up at the University of Franche-Comté thank to the ANR 2005 program. Biotika® has succeeded 5 times to benefit of this kind of financial process (Fibrotika in 2006, Physiotika® in 2008 and 2009, S-Alive in 2010, AgiMilk in 2011).

The Clinical Investigation Centre – Technological Innovations of Besançon (INSERM CIT 808) is located in and managed by Besancon University Hospital and INSERM as co-manager. The Clinical Investigation Centre is approved by INSERM and the DHOS for two activities: biotherapies (CIC-BT approved in 2005 and reconducted in 2010) and Technological Innovation (CIC-IT approved in 2008). The CIC-IT is already implied in medical devices development through ANR and OSEO programmes and translational research. The institute collaborates with the environmental platform MicroTech-hosted by the Health institute of technology transfer of Franche-Comte (Institut Pierre Vernier).

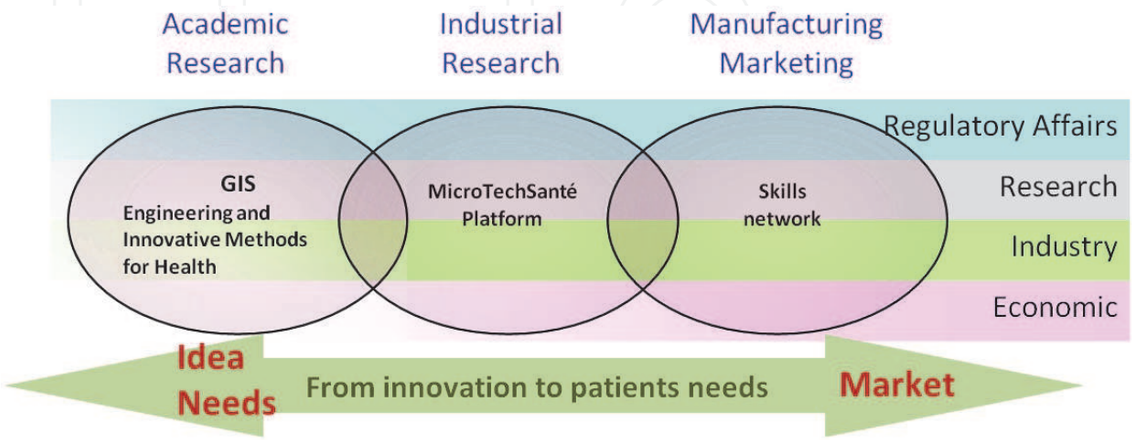


Fig. 1. MicroTech platform principle

Our virtual firm collaborates with the incubator in Franche Comté. Christophe Moureaux, a senior engineer, joined the incubator in December 2009 to set up a company (Cisteo MEDICAL) dedicated to the development and manufacture of new medical devices combining established material, associated motor units, sensors and embedded energy, in partnership with the ISIFC and Biotika® and the University Hospital of Besançon. This start up is now supported by OSEO. The further development of the devices pre incubated by Biotika® will be provided later with Cisteo MEDICAL by consortium.
Biotika®, virtual firm, develops real active partnerships with industrial actors: Cisteo MEDICAL but also Alcis, Covalia, Statice and Technologia. This industrial partnerships' list is undergoing constant. Franche-Comté lies at the heart of Europe, a region in the east of France. The border between Franche-Comté and Switzerland is 230 km long. It's an important factor of our biomedical industrial network's success.

4. Virtual company structure

The "virtual company" works with French collective agreements 3018 but without legal status. The legal status is in fact a university status. The activity is only on 2 days per week and only during 7 months per year. It's in fact an innovative educational concept with focus on real medical devices' conception. The trademarks are INPI registered.
In 2006, students enrolled and whose names are designated in part N°16 in thanks, created all together and in total autonomy (but after validation of management) all communication tools. For example, they create their company name and logo (fig. 2) which were INPI registered in 2007. Now, it's the same process for new products' names. Physiotika® in 2008, S-Alive® in 2009 and Agimilk® in 2010 names were INPI registered.

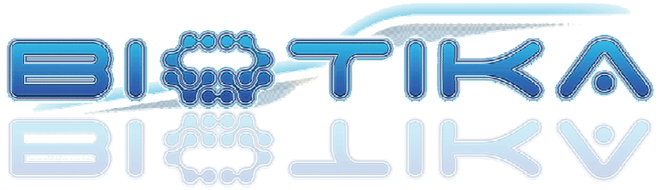


Fig. 2. Logo of our virtual company is INPI registered

The Biotika®'s website is http://biotika.adeisifc.fr/
The webmaster is a student.

5. Management principle

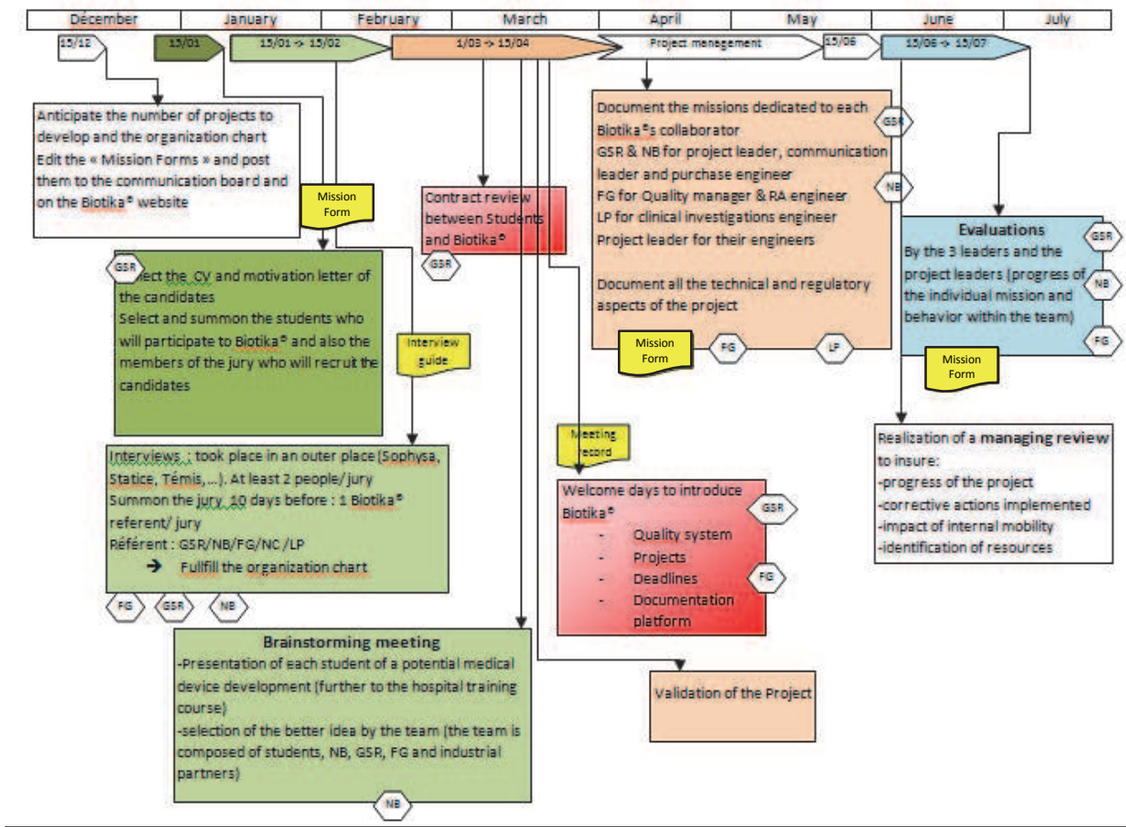
5.1 Innovative principle

Further to the hospital training course (6 weeks), the new members of Biotika® decide together on new projects they want to develop. The objective is to innovate, that means to develop at least one innovative medical device per year. Since its creation, 8 projects were pre incubated. We want essentially to work for patients who are affected in terms of their quality of life and a significant reduction in their disability.

5.2 Steps principle

Principle is described on figure below. We have five steps and two phases during half year 4 and half year 5:

1st phase : half year 4



2nd phase : Half year 5

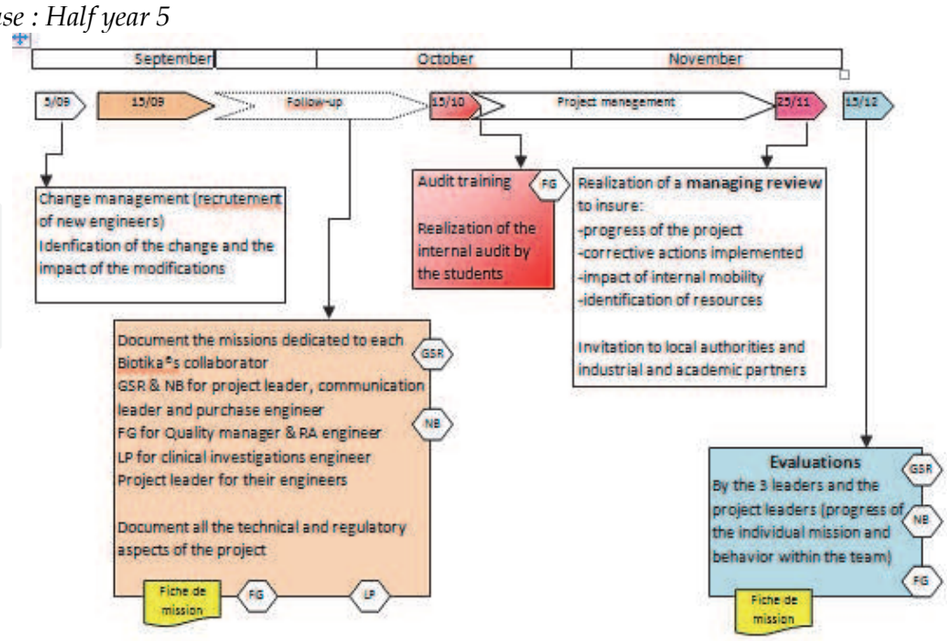


Fig. 3. Management principle during the two semesters, half year 4 and 5

- Detection of needs (after hospital internship) Definition of functional specifications, bibliographic research, relevant economic and clinical benefit / risk
- Research evidence, experiments and simulations of feasibility, design demonstration models of preclinical protocols and files for CE marking, removal of the first scientific obstacles
- Research funding, confidentiality agreements and partnership
- Launch of joint development and validation of preclinical
- Transfer to real companies in the manufacture of prototypes and pre-industrial to industrial

6. Organizational structure

Biotika® team for 2006 was initially made up of thirteen people, including eleven ISIFC engineering students (see list in Part 16, Acknowledgements). Every year, Biotika® staff is completely renewed. All the posts (except management) are attributed to the new pupils-engineers of the 2nd year of ISIFC. They are really interviewed by professional people.
In 2007, the team organization changed. It consisted of eighteen people, including fourteen engineering students ISIFC sometimes with double missions. A department Quality / Regulatory Affairs / Marketing / Communication was created. Technical Director (half part time Human Resources Director) droved three different projects (CP 1-3) and the purchasing manager logistics. Most of them worked in project team (a team leader with R&D engineers by project). Some of them worked with transverse missions or with specific responsibilities (purchase, communication, regulatory affairs, quality, marketing, supplier quality assurance, clinical investigations).

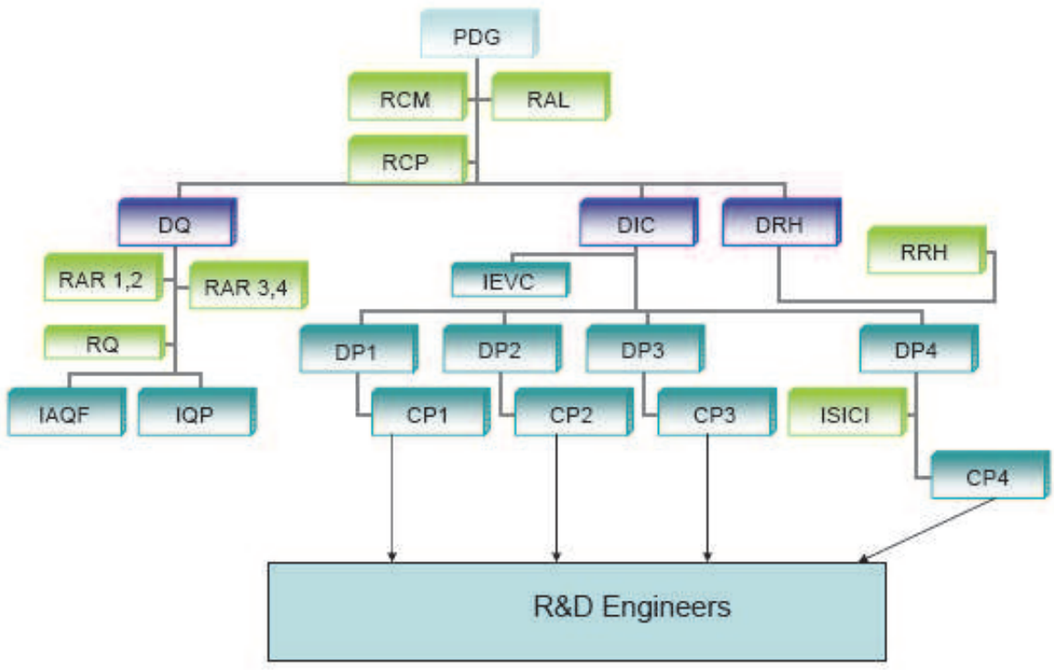


Fig. 4. Biotika® 2008 team

In 2008, the Biotika®'s team (Fig. 4) was composed of 30 persons, including twenty-one students ISIFC engineers. The direction of Biotika® included additional permanent members: a doctor of hospital university CIC-IT department (Dr. Lionel Pazart) as director clinical investigations (DIC), four project managers (DP1 to DP4, Georges Soto Romero, Fabrice Richard, Sébastien Thibaud and Sébastien Euphrasie are all teachers and researchers of FEMTO-ST CNRS laboratory). Each tutorial provides a close with the respective project manager. The new interviews of the virtual firm are outsourced over Statice Santé Company and Témis Institute. It tooks place in Besancon in April 2008 to allocate to each its place within the virtual company and to fill a number of new missions related to the following positions:

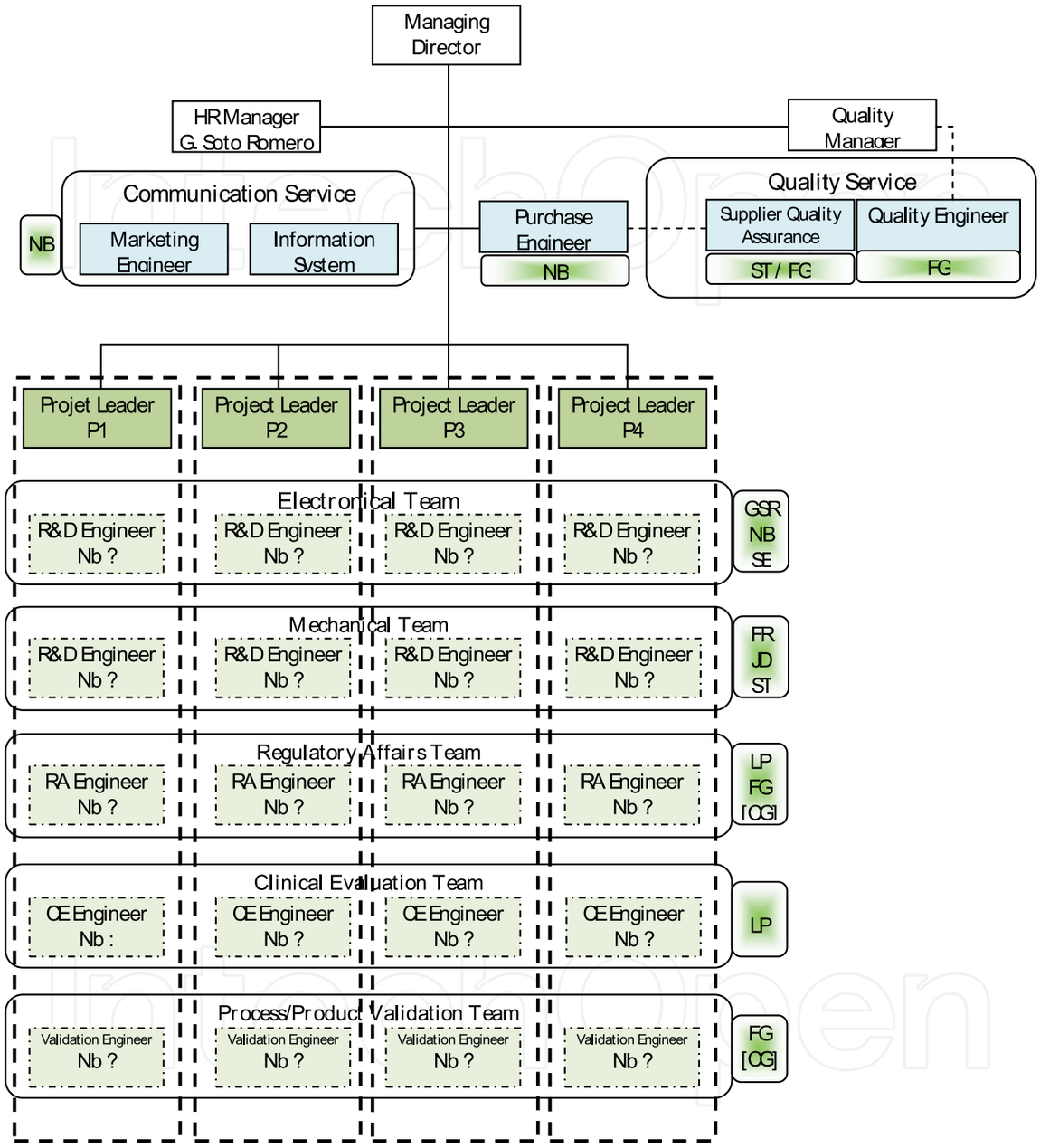
- Four project leaders, CP1 to CP4
- Research and Development Engineers,
- Logistics & Purchasing Manager, RAL
- Communications project manager, RCP
- Communication / Marketing, RCM
- Quality Manager, RQ
- Regulatory affairs Manager, RAR
- Quality assurance manager with suppliers, RAQF
- Product qualification engineer, IQP
- Information system engineer-collaborative platform and internal communication, ISIC
- Clinical testing and validation engineer, IEVC.

The offices of Biotika® are located in the premises of ISIFC in Besançon. Their members have access to the technological and logistical resources of FEMTO-ST, University of Franche-Comté, ISIFC, Besancon Hospital and CIC-IT. A platform of engineering collaborative allows a technical partnership with schools of Morteau and Dole. We work nearby the IUT (University Institute of Technology) in mechanical engineering as well as the AIP Primeca of Besançon. Thus, all pieces are manufactures in Franche Comté region.
A PLM tool is used to share the different documents generated by the students during the R&D process.



Fig. 5. ISIFC/Biotika® building located on TEMIS Park and managing revue meeting

Now, managing director uses a cross matrix described bellow.



The legend is for the permanent staff:
NB : N. Butterlin, GSR : G. Soto Romero, FG : F. Guyon, LP : L. Pazart, ST : S. Thibaut, SE : S. Euphrasie, JD : J. Duffaud, FR : F. Richard, [CG] : C. Garcia.
The general organization is composed of permanent staff and there is one project manager by project. All the others functions are assumed by students. Their number depends on complexity and project. There are mechanical and electronical R&D engineers' teams.

Fig. 6. Crossed matrix, organization chart functional

7. Innovative active training

7.1 Missions of the training module

This is, in a virtual firm, to create and maintain a dynamic coaching and collaborative work that gives students opportunities for implementation of academic knowledge in biomedical engineering. The purpose is to provide students and this during their training, a scenario first real experience "tutored" and participative management style. They discover in their future learning progressive industrial activities.

This allows students in terms of autonomy, initiatives and recovery:

- To highlight their individual skills (know-how and skills: passion for work and for other people especially patients….),
- To correct their shortcomings and provide a true assessment of skills
- To involve them fully in the development of image with:
  - Companies in the biomedical sector,
  - Hospital centres,
  - Local, regional, national and international institutions of higher education or secondary technical and regional operators,
  - Students from Faculty of Medicine,
  - Patients associations.
- To have ideas for innovation
- To be able to develop innovative medical devices

After the module, they know that innovation takes a lot of time, a lot of energy, a lot of creativity and needs strong interactions between mentors, mentees and many others.

7.2 Resources available

This module is expected late in the second year (semester N°4) and the beginning of the third (semester N°5). It is built on a base of 7 European Credit Time System (ECTS) or 175 hours in terms of teaching model. It is divided into two parts: a form of 3 ECTS in semester 4 (Number of Hours: 8 h classes, Individual Project Time 67h) and 4 ECTS in semester 5 (Number of Hours: 8h classes, Individual project Time 92h). These hours are: controlling and monitoring of the "virtual firm", the organization and implementation of recruitment in offshore locations, the organization of "events" such as progress meetings, quality audits technical and internal customer visits and / or suppliers, participation in trade shows ...), organization and implementation of talks progress and interviews. It must include a plan for internal training in innovation, clinical trials, programming microcontrollers or finite elements, internal auditing, first aid, ...

The "budget schedule" of compensation for the part of teachers entrepreneurship varies from year to year: it partly depends on the training plan (action contractors) and "consulting" done by specialists from Biotika®. A "system standby" (on the model of hospital guards) is being implemented for the management team and rewarded accordingly. The "maximum budget" available for payments of permanent staff and / or individual contractor is calculated on the basis of

1 group / 24 students and 1 group TP / 5 students.

A teaching group of at least 6 people for the management team and technical supervision is necessary for steering Biotika®. It consists of permanent members of the ISIFC who are at least one specialist in quality (DQ), a specialist in research and R & D (PDG), a human resources manager himself a technical expert (DRH and DT) and a specialist in investigations clinical

DIC. The four students project managers (P1 to P4) act as intermediaries between students recruited technical and management Biotika® staff. The support by "consultants" in optics, mechanical and electronic designs, marketing and business plan (participation of university companies' management school of Besançon), medicine allows students to have recruited ad hoc support. The supervision of the training module Biotika® Entrepreneurship is thus a specific and custom framing increased. It's a real experimental innovative educational program.

7.3 Activities associated with the module

For each project developed, it is:
Design and implement a technology demonstration vehicle (or functional model) of a biomedical device. So get models' skills students ISIFC "for trade shows, national day" Celebrate Science "forum of students, JPO ...
Introduce a quality approach in designing a medical device in collaboration with technicians and / or operators, according to the standard ISO 13485.
Conduct a market analysis and research prior art product.
Conduct a comprehensive study in order to obtain the CE mark.
Conduct research and transfer of technological device designed to a manufacturing process in collaboration with secondary schools, technical platforms and / or regional IUT.
Implement corrective action following audits to ensure the quality policy of the company.
Learn self-assessment and / or evaluate its partners know how to respond to questioning skills assessments.
Learn to understand the needs of businesses in terms of qualifications, with a good-looking management of the student's career.

8. Building the appropriate team and managing people

Every year, Biotika® renews its staff (excluding permanent management) and no period of recovery is possible! A real campaign is organized. The process is conducted with multiple conversations between individuals. It's after Internet publication by firm's website posting. The candidates are selected by pre-processing of curriculum vitae and cover letters in French and English. Lasting about one month, ten recruiters are necessary for the recruitment operation. This year, 47 candidates are examinated for 23 jobs. Between recruiters, they are: manufacturers (and in fact also ISIFC engineer graduated), consultants, permanent Biotika®'s staff. The recruitment locations are offshore (business partners or local business incubator). All aspects of a job interview are discussed and a response to each application is made (the call to service or not, positive / negative). The final allocation of posts is based on current skills but also detected (refining the professional project of the student). This is the moment to initiate a real active support success.
In March as is explained in Figure 3, each student turnover, innovative projects are proposed and discussed by staff Biotika® (permanent and students). Then, the final choice is made by all staff but with a constraint: only one has to be new and innovative. The other projects will be developed in continuity with the previous team and with at least one of them, specifically oriented biomechanics.
House training specific to programming microcontroller is available to all. A second phase of internal training is then carried out by Internal Audit.

Individual interviews with each student assessments, both technical and position are made in late June and late November by the N +1 and permanent managers. The rating and credits obtained allow validation as an engineer graduated from ISIFC. A review of activities, such general meeting and open house, are presented every year in late November to the major partners.

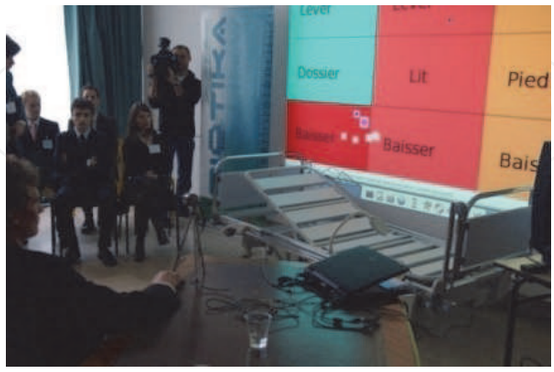


Fig. 7. Managing revue meeting.

9. Patenting, trademarks and copyrights

The patenting and intellectual properties are very important for the general manager of Biotika®. The university valorisation framework supports Biotika®'s projects by different processes:

- Negotiating and writing the consortium agreements,
- Implementing conventions (recruitment, managing expenditure and receipts, sub-contracting),
- Following ANR programme implementation
- Closing conventions and producing administrative items justifying expenses.

Valorisation University Department ensures in particular that the results of the project are protected, if necessary by submitting a patent, as well as commercial valorisation by identifying the partners likely to take out user licenses.

The INPI is the national institute for intellectual and industrial properties registrations. The original and innovative concept of our "ISIFC's virtual firm" can't patent. But the mark and logo of Biotika® are INPI registered on four classes: N° 09, 10, 41 and 42 with specifications detailed bellow:

- Class N° 09: Devices and instrumentations for scientific research in biomedical engineering domain.
- Class N° 10: Devices and instrumentations for surgeons, physicians and biomedicines. Beds for healthcare, endoscopes, fibro scopes, saliva automatic distributors….
- Class N° 41: teaching and professional training services for biomedical engineering students.

The community law requires a use of the brand «in the life of the business" that means according to the community case law «the exercise of an economic activity ", " the offer of the goods and the services on a market " or " the exercise of a commercial activity aiming at an economic advantage ". The name of the class 41 thus asks question: does the training service proposed by the ISIFC raise of the life of the affairs? Yes, because we consider that

the training is paying and that there is a "market" of engineering schools (competition to recruit the bests "pupils-customers")

- Class N° 42: Scientific and technologic services for biomedical engineering domain (medical devices, instrumentation). Research studies and developments services are included.

Biotika® INPI registered 4 Soleau letters and 3 marks and worked on 4 anteriority studies.

10. Documentary and communications system

Within Biotika®, which remains a young company, all the staff is involved in the communication strategy of the company. By this approach, the management team expects from every student that he learns to communicate with various interlocutors (MD, senior engineers and customers). But also, because of the renewal of all the staff from one year to the next, the written traceability of all the activities, the technical choices on each project and the whole life of the company must be guaranteed by each staff member.

External communication:

This requirement justifies our choice of using, more than a web domain (biotika-isifc.com) in which we can store our website, a new communication and networking platform, Agora Project. We found in it a reliable an easy handling tool for collaborative engineering.

Agora project allows sharing all useful information with our different partner, such as Morteau and Dole schools (mechanical drawings, printed circuits board designs). In that case, Agora is used as a powerful external communication tool.

Internal communication:

Agora project is also an internal communication tool, used as same as an intranet. Memorandums, agendas and meeting reports are uploaded and shared with all the staff.

The quality system of Biotika® requires a lot of data records. We can use Agora Project as a distant storage server, and a HR resource tool (for new staff members, holidays planning, etc).

Best results :

This network based communication system help to increase our productivity. Also, our students were able to contribute on scientific production (papers, posters) related with each project and with the firm. In the other hand, they could participate on several meetings like Micronora (3 times since 2006) and MEDTEC France (2 times since 2010).

11. Quality management system

11.1 Quality policy

In addition to train students for the workplace, Biotika® has its own goals as a company whose virtual goal is to improve the lives of patients:

- Develop and implement innovative medical devices,
- Establish a quality system for the company according to ISO 13485,
- Conduct a technical file on each product,
- Assume the investigations and clinical trials for a CE
- Ensure internal / external communication of the company, market analysis
- Managing the company in its entirety: budget, employment contracts, quality audit, meetings with industry, intellectual property, ...

- To transfer the concept to an academic or industrial partner able to guarantee production (mission partnership, quality file) or create a real business.

The quality process unfolds within any organization Biotika® (structure documentary records in relation to the requirements of ISO 13485). Every years, actions are validated through an internal audit carried out in the end of annual activity.

Quality Policy of Biotika®

BIOTIKA® aims at developing medical devices and improving the industrial and academic partnership. Also Biotika® makes a commitment:

- To implement a case study
- To reach the missions defined at the beginning of the project
- To give a new approach of the entrepreneurship
- To implement the engineer's sciences learned during the year
- To allow the students to integrate the industry dimension
- To transfert the knowledge to the following promotion and so to maintain a dynamic within ISIFC
- To facilitate the professional insertion
- To implement the partnership with local schools
- To insure the recognition of BIOTIKA® by the professional of the biomedical area and by the local authorities

As managing director, me, Nadia Butterlin, I make a commitment to give all the resources necessary for the good functioning of BIOTIKA®. In order to meet all biomedical industry aspects, I named a quality manager who is in charge of the Quality Management System according to the ISO 13485 standard.

Nadia Butterlin
Managing Director

Fig. 8. Quality policy of Biotika®

11.2 Processes and mapping

At the beginning, the main important step was to identify the customers and their expectations. It was not simple to define the main customers to satisfy. The direction decided to satisfy in first the student themselves.

One of the first actions initiated by the student was also to identify the processes which would have an impact of the customer's satisfaction. For them, there were 2 main activities:

- **Communication** : in order to become known Biotika®
- **Design** : in order to develop the innovative medical device chosen

To monitor these 2 processes, a management process is there to define the policy, to engage the corrective and preventive actions, to audit the system in place and to review at an adequate frequency the aptitude of Biotika® to meet customer's requirements during managing review.

And to support the realization processes, some activities were precised as:

- Documentation management
- Purchasing actions
- Incoming inspection
- Measuring instruments monitoring
- Regulatory survey

The students after the processes identification decided to map them in order to define the interfaces between each process.

Another important action was to define the documentation (describe all the procedures of the quality system) and the record necessary to prove that the activities are implemented according the quality system in place.

An internal audit is performed every year and two management reviews are led to insure that the system of quality management is conform to the ISO13485 standard. The implemented actions are reviewed and also the objectives. The evaluation of the "employees" validates the obtaining of the engineering degree of ISIFC.

You can find below the map which is also in the Quality Manual

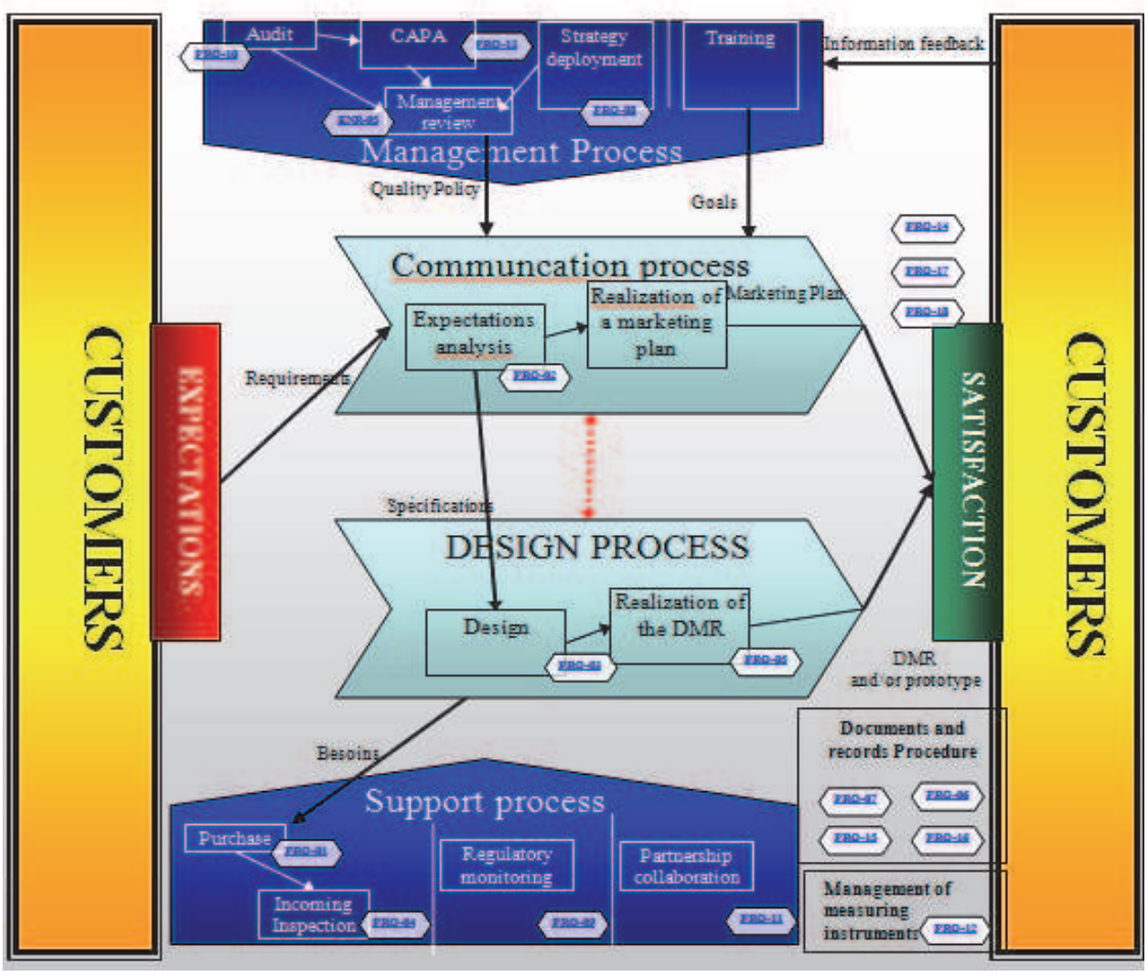


Fig. 9. Quality Map

12. Maturing projects' story

Within Biotika®, two products were developed in 2006: a bed voice-activated and an automated flexible endoscope. This year, there are five different projects.

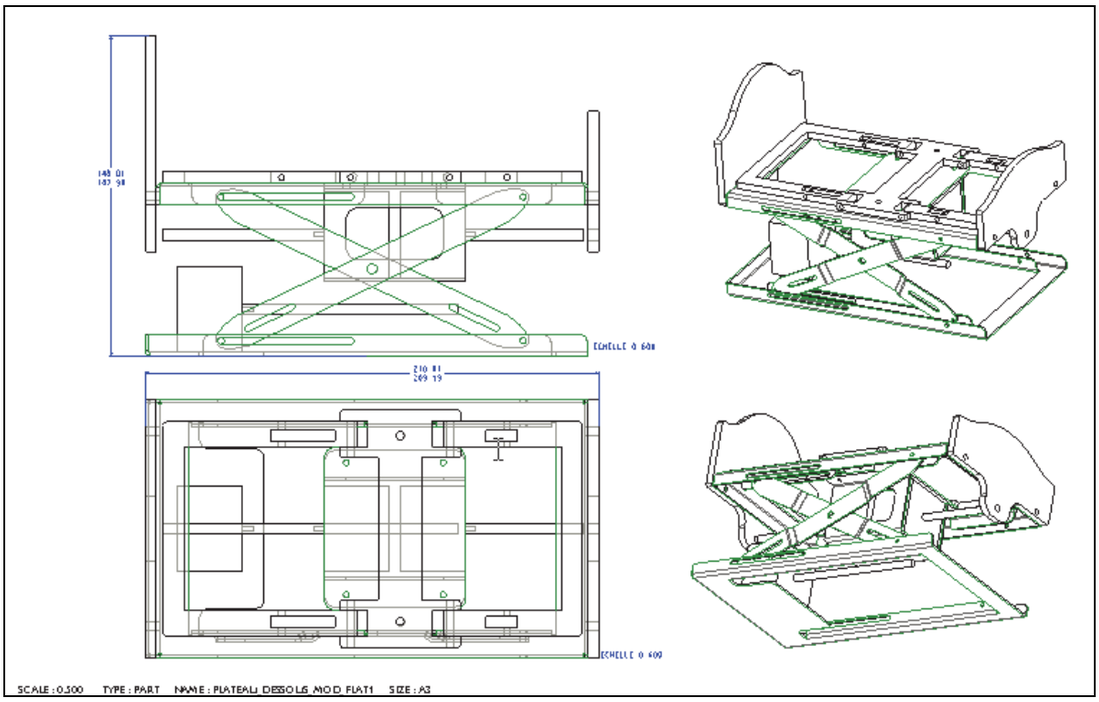


Fig. 10. Manufacturing plans exhibited at Micronora 2006

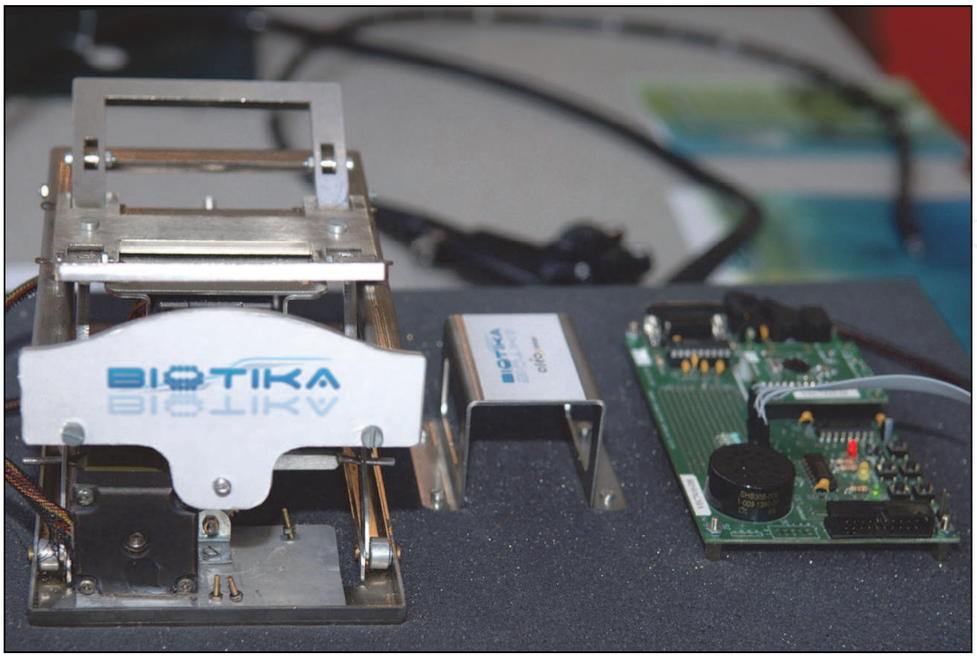


Fig. 11. Working model exhibited at Micronora 2006

12.1 Hospital bed with voice recognition

The concept is based on the instrumentation of a motorized hospital bed to a patient or the caregiver to control the position of the bed by voice recognition. Instructions, recorded in advance, allow engines to operate the corresponding control. Possible instructions are "up" and "down". They can then be combined with "whole", "head" and "feet". To ensure the functionality of the bed, an alternative means by remote control manual has been planned.
A working model shown in Figure 10 and based on the principles outlined above was performed.

12.2 Automated flexible endoscope

The concept is based on remote instrumentation, using a joystick and miniature motors, displacement of the head of a video endoscope (a variety of flexible endoscope) which is used in the exploration of some cavities body and the taking of samples. To date, this shift is based on mechanical action at the end of an endoscope through knobs. A wheel provides the lateral movement of the endoscope head and the other the vertical displacement, which makes the system cumbersome. However, this system has many disadvantages for the user. Originally intended to be manipulated with one hand (while the second deals with the insertion and withdrawal of the endoscope), this is not the case in reality. Indeed, it is found to be extremely difficult to use simultaneously, with ease and precision, the two control knobs with one hand.
There are two solutions to the practitioner:

- Use both hands to control, requiring the presence of a third hand for insertion and withdrawal of the endoscope (nurse)
- Or use only one of two dials (most accessible) with one hand and rotate the 90 ° endoscope to access the other direction.

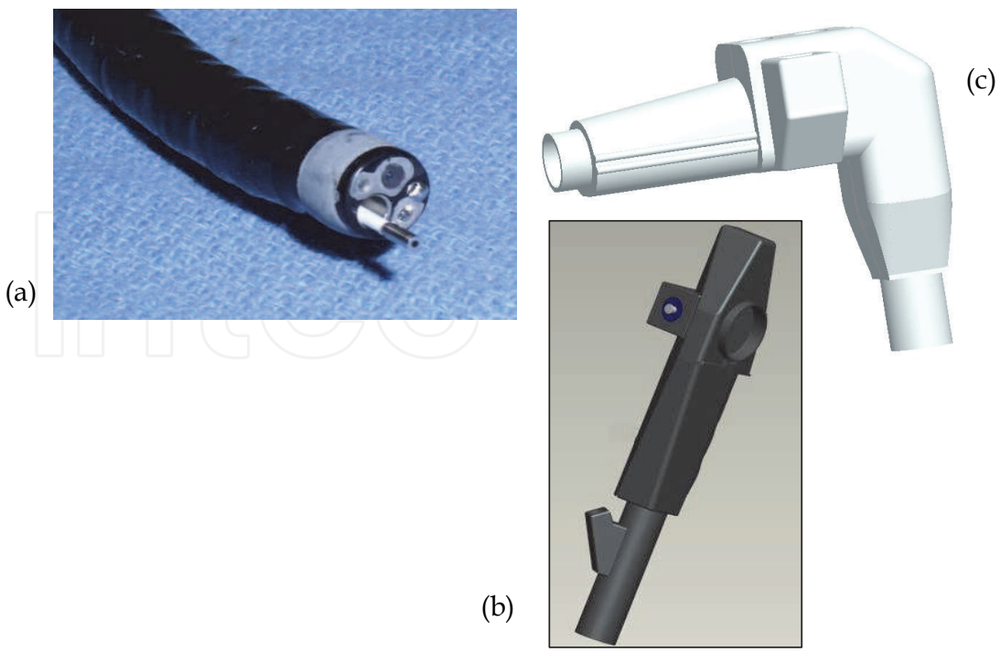


Fig. 12. (a) Head of the endoscope control ,(b) Model of the proposed handle with joystick, (c) handle being designed

If, to maintain total control of the procedure, experienced practitioners have mastered the second method presented above, this is not true of young interns who need lots of practice before they can act alone. This problem of handling the endoscope, it is clear: an increase in the time of the intervention, a greater risk of irritation or perforation of the walls for patients (especially during this period of learning internal) and an increase in the learning period of the endoscopic technique.
This study on improving the ergonomics of flexible endoscopes has led to Biotika® proposes as a solution to automate the order.
A feasibility study was undertaken in partnership with the Division of Gastroenterology CHU Besançon and Dr. Stéphane Koch. A first demonstrator has been realized in 2006.
In 2007, the new team has developed the product automated endoscope, Fibrotika renamed, and worked in parallel on two new projects: Visiotika, a device for visual control interface for controlling the environment for people paralyzed and S-Alive dispensing device of artificial saliva for patients with xerostomia (destruction of the salivary glands).

12.3 Fibrotika: Following the project automated flexible endoscope

In 2007, Biotika® decided to continue the project renamed Fibrotika automated flexible endoscope. The goal is to move from a demonstration model named by students Simulscopie at a pre-prototype used for preclinical trials. The tests are scheduled at the University Hospital in late 2008 (R&D internship, L.Debar). Contacts with companies specialized in the design and manufacture of endoscopes have been established. The ability to add sensors at the end of the sheath of the endoscope to create a force feedback on the action of the command, and the development of a simulator test to measure efficacy are studied. Anteriorities' research results and the important fund needs are the two major reasons to stop the maturation process of Fibrotika inside Biotika®.

12.4 S-Alive ®

This project involves the development of a new distributor of artificial saliva for patients with Xerostomia (dry mouth sensation) and / or Asialia or oral dryness (lack of or decrease in production of saliva). These patients can not produce saliva following a destruction of the salivary glands usually secondary to radiation therapy. The result is pain everyday that degrade the live of these patients. There are currently sprays and gels to fill the lack of saliva, but these solutions do not allow the patient to receive the saliva continuously.
The anticipated benefits for patients are: greater autonomy, improved quality of life, particularly in the context of social life and greater discretion with respect to the other people and finally an increased efficiency on oral complications and comfort due to direct and regular administration of the substitute on the oral mucosa and dental tissue.
The main investigator of this project is Dr. Edouard Euvrard (INSERM CIT 808 - IBCT INSERM UMR 645). The hospital coordinator manager is Professor Christophe Meyer. He supervises research program and he's Head of the Department of Oral and Maxillofacial Surgery at the University Hospital of Besançon. They are responsible for the definition of specifications (including the physiopathologic aspects) and the surgical acts during pre-clinical studies in animals. They are responsible for writing up intermediary reports and the final report. The study will take place in the department of maxillo-facial surgery of Besançon CHU. The CIC-IT will carry out the necessary administrative steps (writing and submitting a file to the committee for the protection of persons in the East of France, for example), conducting the study and the statistical analysis of the results.

In 2007, project begun with an ISIFC hospital internship. In 2008 and 2009, several steps were taken by Biotika®: defining specifications and technical, pre-record risk analysis, designing a virtual model in CAD with SolidWorks and SpaceClaim, then building a demonstrator incorporating a miniature peristaltic pump alarm with a battery and for filling (PCB feasibility demonstrator, see bellow).

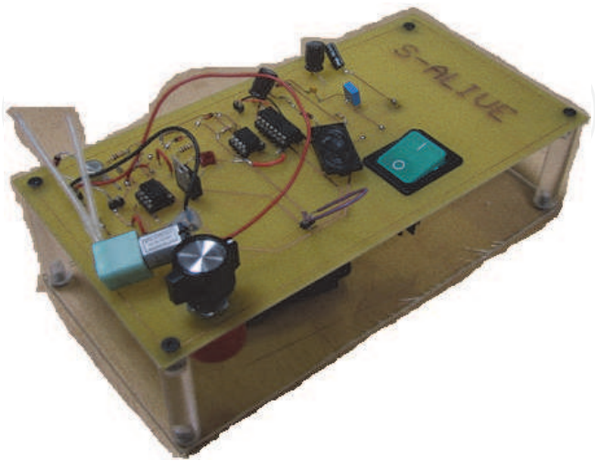


Fig. 13. Feasibility experimental demonstrator

A first patent search (December 2006) led to the submission of a Soleau envelope (Dr. Edouard Euvrard INPI N°305818, December 6, 2007). Recently, with new patent search of March 2010 (ARIST), five competing patents were identified: they are mostly North American with one from France. These patents were not considered a threat to our device by ARIST. Such a device is not currently on the market and the priority analysis shows that freedom to operate and patentability is possible for our idea.
Before the S-Alive ANR project, which has just started, the valorisation framework had already contributed to the realisation of a pre-study, with en amount of 25.000 € through an innovating project maturation fund in 2010. This OSEO-Maturation project names "Substitution of the insufficiency or absence of saliva in patients suffering from xerostomia" and is coordinated between ISIFC/Biotika®, Besancon University Hospital, Department of Maxillo-Facial Surgery, CIC-IT, EA4267 Biologic separative sciences and pharmaceutics laboratory and Vetagro-Sup animal's school and its external providers (Cisteo MEDICAL and Statice Santé firms). A market analysis is also planned for, as well as the realisation of prototype tests on animals to evaluate the risks associated with using this type of device.

12.5 Visiotika

This project aims to enable completely paralyzed patients, such as those suffering from Locked-In Syndrome, to regain some autonomy by giving them the ability to control their environment through their eyes. Currently, such solutions exist but are extremely expensive. Biotika 2007 has made such a device at low cost by simply using common materials. Thus, Visiotika consists of a webcam connected to a laptop quite commonplace, free software easy to use and infrared connections for connecting the PC to control the elements. The motivation is to enable patients to purchase this device for their home. The eye movements of patients captured by the camera can act on the software as you would with a computer mouse. The information is then sent via IR wavelengths to different parts of the patient's

environment. Visiotika can control a TV and the hospital bed set up by previous team. It can be easily adapted to other applications, such as the opening of electric shutters, turn on and off the lights...This project is in stand by for the moment.

13. Physiotika® project 's description

Physiotika®, was developed to measure pulse wave velocity, a strong predictor of cardiovascular risk. This innovative device measures pulse wave velocity by using two infra-red probes, placed on two artery sites.

Increased arterial stiffness is associated with an increased risk of cardiovascular events. For example, in patients with chronic renal disease, this risk appears to be far greater than in the general population. Several methods are available to determine arterial stiffness, and pulse wave velocity (PWV) appears to be the most accurate. The current gold standard to measure PWV is through applanation tonometer (AT).

Non-invasive and predictive of adverse cardiovascular outcomes, this device is technically challenging and expensive. However, Physiotika®, a non-invasive method, uses the principle of reflectance PhotoPlethysmoGraphy to detect cardiovascular pulse waves. This is a common optical technique used to monitor peripheral pulsation.

The Physiotika® device described bellow is composed of

- specialized software program (1)
- housing containing a microcontroller (convert the analogical signal into a numeric signal) (3)
- USB cable to connect the housing to the laptop (2)
- two infra-red probes (carotid and radial) (4 and 5)
- neck support to secure the carotid probes (6)
- wrist support to secure the radial probe (7)

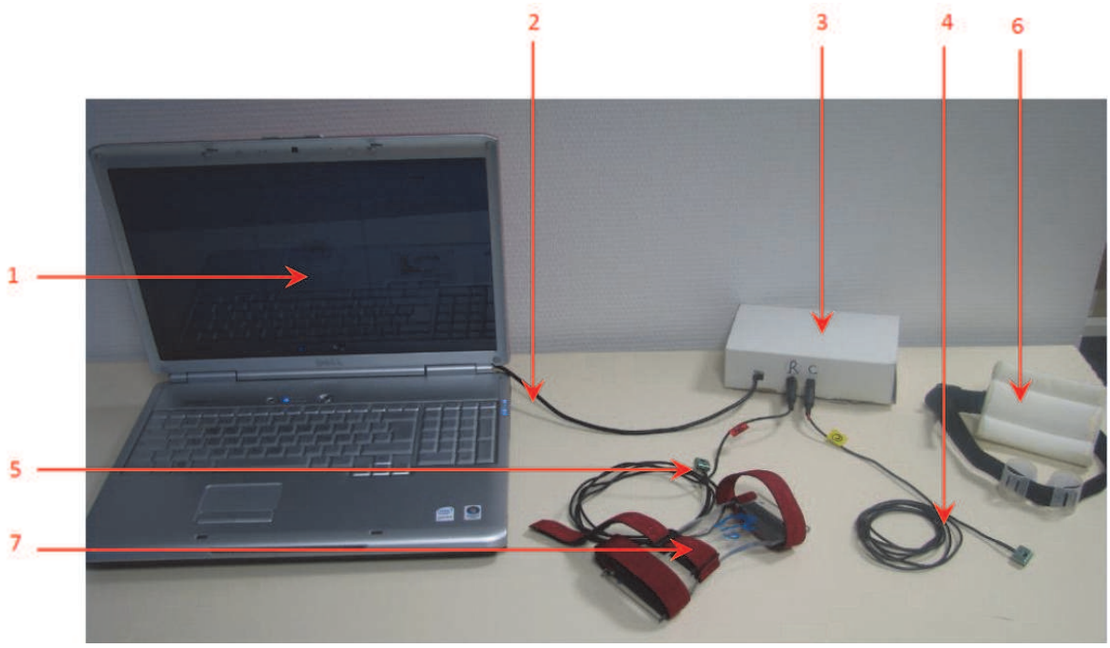


Fig. 14. The Physiotika® device

Three different Biotika® teams (managed firstly by J.Imbert, secondly by C.Soulaine and V.Journot and lastly by B.Jacob) have shown that this new device is able to measure a valid index of PWV, as compared to the AT technique in healthy subjects. This project has been technically established but requires continued validation in a clinical population. This year, we decide to extract this project from Biotika® and to transfer 3 prototypes to researcher partners for new international experimentations (in Venezuela and Colombia) and new campaigns of data's collect.

14. Pre-clinical validations process and regulatory affairs

In fact, Biotika® is able to conduct:

- Technical and preclinical studies
- Technical and preclinical trials
- Technical and preclinical validations

An important vigilance is conducted in these phases.

When we are developing or modifying a medical device, it needs to perform clinical but also animal trials to obtain scientific datas that demonstrate the safety and effectiveness of the new device. When the device is a class I or class IIa classification, it's possible to prove these by bibliographic data. Biotika®'s team can demonstrate scientific and technical concepts and also it can clinical validate the device with simulations and animals trials. We use medical and computing data Center and data research Bases of the University. The clinical investigation works out a contractual arrangement with the teaching and research Hospital of Besançon University (Centre d'Investigation Clinique, CIC). The CIC sponsor (Doctor Lionel Pazart) is responsible for selecting investigators, submits research protocol and human care assurance.

14.1 Example of Physiotika® Investigations

This example of investigations are conducted by a student, J.Picouley, during her 3 months R&D intership. It was just after Biotika 2009 exercise and a previous 2008 R&D internship (N.Mathias).

It was located in the Clinical Renal Investigation Unit at the Kingston General Hospital Satellite Dialysis Clinic, in Kingston (Canada). Trisha Parsons, Assistant Professor, School of rehabilitation therapy at Queen's University was the tutor of this intership. It's an important collaboration with Nicolas Tordi, general coordinator of Physiotika® project. N.Tordi is professor at the University of Franche-Comté and works with ISIFC. The purpose of this study was to determine the test-retest reliability on healthy volunteers and to perform a pilot assessment of the response to change during dialysis. Preliminary results suggest that the Physiotika® device may offer a reliable, low-cost alternative for the clinical assessment of PWV.

Renal failure is associated with an increased prevalence of cardiovascular morbidity and mortality. Arterial stiffness, as determined by pulse wave velocity, is predictive of adverse cardiovascular outcomes such as left ventricular hypertrophy, heart failure, hypertension, and cardiovascular related mortality in the population with kidney disease.

The current gold standard method for assessing arterial stiffness is through the use of applanation tonometry. This method is highly skill dependent and results in difficulty pooling data from different examiners. Given the logistic considerations with subject recruitment, it has been postulated that an alternative method of determining pulse wave velocity using infra-red technology, may provide greater inter-tester reliability.

14.2 S-Alive example

The animals' laboratory, Vetagro Sup in Lyon, works with us for animals trials. If the trial doesn't involve significant risk for patients, a patient consent forms is only necessary to collect clinical datas for human use. The trials and validations campaign conduct to the risk management report in accordance with regulatory expectations.



Fig. 15. Professor C.Meyer, Doctors E.Euvrard and L.Pazart , S-Alive mean coordinators and Biotika®'s partners. First tests on animal monitored by Vetagro Sup.

S-alive project is an active implantable medical devices [AIMD] requiring surgery. Our device will be part of the class IIb Rule 8 (EC Directive 2007/47). Sole responsibility of AIMD's manufacturer is subjected to obtaining the CE mark in "essential conformity" with health and safety requirements set by EU directives (93/42 / CE for medical devices 90/385/EEC). And in this context, the most complex issue in order to obtain the CE mark will remain "the risk management analysis" according to EN ISO 14971:2007 which is mandatory provision. Biotika®'s team participates to the product development with Hospital of Besançon and Cisteo MEDICAL company. The ANR's purposes program is to qualify "the risk / benefit ratio" by referencing all possible risks associated with the physical characteristics of the device, its use before and during manufacture, predictable external influences, medical or surgical procedures, ionizing radiation (sterilization due to radiation), a fault or aging of the device.

15. Conclusion

In the scope of a new module, the ISIFC launched in May 2006 its own virtual company, named by students Biotika®. Virtual means that this company has no real legal status. It is a sort of pedagogic model but on the other hand, the situation scenario for the ISIFC student engineers is itself indeed real. They are currently working-in real conditions-on the development of new medical devices or on modernization of medical products. The needs of these innovative medical devices were identified by the students during their second-year (6 weeks) work experience in hospital. Every year, this activity takes place between March to December. The end-year students were recruited following an imitation job interview and

each of them was entrusted with a mission (engineer or project manager) in one of the company's four departments; R&D, Quality-regulatory affairs, Clinical investigations and Public relations-marketing. Every two days per week and for seven months, the personal of Biotika® works on development of innovative medical devices and on the preparation of CE marking or FDA. Biotika® developed **eight products since 2006.**

Biotika® works on medical devices development projects and on research for patients and clinicians. It became in 5 years a real academic pre incubation cell. Firstly, Biotika® was awarded a financial prize of 15.000€ by the OSEO Agency and Valorisation Department of the Besançon University (maturation funds). It was in June 2006. The youth chamber JCE allowed to our virtual firm participating in European competition for the innovative company in category INNOVACT Community (Reims, October 2006). We participate every year to industrial meetings such as MEDTEC FRANCE and MICRONORA.

We obtained:

- In 2009 a real partnership with Besançon University Hospital's CIC-IT
- In 2010 a real partnership with Cisteo MEDICAL, start-up created in Besançon
- By 5 times, financial support given by OSEO/UFC Valorisation Department

These supports in maturation of innovative projects were intended for the pain and salivary disorders treatment, and for the gastroenterology and cardiovascular diagnosis.

- 5 clinical trials
- 9 R&D and hospital ISIFC internships

Recently, the selection to the ANR (National Agency for Research) is going to allow developing industrial prototypes of technical substitution of saliva for the maxilla facial cancer research with Besançon University Hospital, EA 4267 Laboratory, Cisteo MEDICAL start up and Lyon animals' school. For this 2010 ANR campaign, only 30 projects are selected and obtained 2 years financial support for 271 national candidates.

For the moment, no Biotika®'s product is still marketed. Two patents are in the course of writing, 4 Soleau Letters are INPI registered. The main difficulty is not due to unavailability of the students, in contrary! They are principally due to their irregular presence (discontinuity in the time) and by students coming from different promotion. And for the development of innovative projects, it needs real industrial partnership for a potential transfer. Furthermore because the staff is completely renewed, the transfer between the 2 teams is a critical process and requires a documentary system exemplary.

Very recently, we obtain funds from Franche Comté Economic Chamber (Intelligence Agency) and from University for a real LNE/GMED ISO 13 485 certification. The first audit will be in November 2011.

Three options are selected for Biotika® 2012:

- keep our original and innovative ISIFC's university Biotika® virtual company concept and move every year new ideas and technology to other partner companies (for conventions).
- actually create a company with the status "Thurs Young Enterprise University" (Biotika® 2011 engineering students involved will graduate in July 2012).
- create a "junior company"with 1901 association legal status and for convention with the engineering school ISIFC which currently has 144 students.

Biotika® is in fact a university structured process for helping patients, clinicians and researchers turn a good idea into a viable medical device business.

Biotika® is not a real firm but it's a real innovative education program for graduate excellent biomedical engineers able to develop real innovative medical device.

16. Acknowledgments

The "virtual CEO" would like to thank especially, in agreement with its management team, the eleven co-creators of Biotika. These student engineers / contractors, graduated in 2007, are now working for the real tasks of development and marketing of medical devices for patient care. Firstly, they were: Khalid Azzouzi, Anthony Bataillard, Amandine Botella, Jérémy Degrave, Florent Demonmerot, Emmanuel Gantou, Cyril Gamelon, Mathieu Guillaume, Marie-Claire Leve, Davy Ung and Yohann Viennet. Thank course the young and dynamic who is now provided by all engineering students/Biotika® engineers of ISIFC: the last but not least 2011 Biotika® team (23 students)! But, I particularly want to express my gratitude to 2007, 2008, 2009 and 2010 teams which represent a total of 89 different students. I would have been able to list all their names! Sébastien Thibaud, Sébastien Euphrasie, Nadège Bodin Courjal from FEMTO-ST institute and Jacques Duffaud (ISIFC studies director) and Christophe Moureaux are our scientific experts. Magaly Roy and Mohamed El Hamdaoui are always presents for helping our virtual firm and in fact our students. Sincerely thanks to them. I don't forget our major Besançon's hospital Collaborator Dr Lionel Pazart and his colleagues and physicians and/or researchers: Professors R.Aubry, E.Euvrard, S.Koch, C.Meyer, A.Menget, G.Thiriez, J.Regnard and N.Tordi. This chapter would not have been possible without the enormous support from Georges Soto Romero and Florent Guyon.

17. References

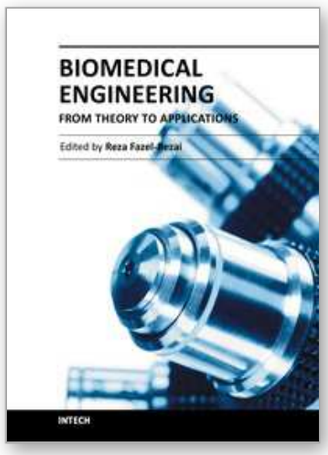
O. Blagosklonov, G. Soto-Romero, F. Guyon, N. Courjal, S. Euphrasie, R. Yahiaoui and N. Butterlin, *Virtual Firm as a Role-Playing Tool for Biomedical Education*, Proceedings of the 28th IEEE EMBS'06, Engineering in medicine and biology conference, New York city, USA, Paper SaC 14.3, pp 5451-5452, August 30-Sept 3, 2006

N. Butterlin, *Biotika students put to the test at a virtual school*, Reference innovation N°5, pp 64-67, November-December 2006, (invited paper)

N. Butterlin, G. Soto-Romero, J. Duffaud, O. Blagosklonov, ISIFC, *Dual Biomedical Engineering School*, Proceedings of the 29th Conference of the IEEE Engineering in Medicine and Biology Society, Lyon, paper FrC12.1, pp3098-3101, August 23-26 2007

N. Butterlin, G. Soto-romero, F. Guyon , *L'entreprise virtuelle Biotika de l'ISIFC ou les grands principes d'une ingénierie pédagogique innovante en relation directe avec les entreprises*, EdP Sciences: J3eA 8, 1024 (2009), DOI: 10.1051/j3ea:2008065, Access Jan. 2009, Aavilable from http://www.j3ea.org/10.1051/j3ea:2008065

A. Moreau-Gaudry, L. Pazart, *Développement d'une innovation technologique en santé : le cycle CREPS, Concept-Recherche-Essais-Produit-Soins*, IRBM 31 (2010)12-21, Biomedical Engineering and Research, Elsevier Masson, Access Feb. 2010 , Available from http://wwwsciencesdirect.com



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In all different areas in biomedical engineering, the ultimate objectives in research and education are to improve the quality life, reduce the impact of disease on the everyday life of individuals, and provide an appropriate infrastructure to promote and enhance the interaction of biomedical engineering researchers. This book is prepared in two volumes to introduce a recent advances in different areas of biomedical engineering such as biomaterials, cellular engineering, biomedical devices, nanotechnology, and biomechanics. It is hoped that both of the volumes will bring more awareness about the biomedical engineering field and help in completing or establishing new research areas in biomedical engineering.

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