



INCDCF- ICCF Bucharest

Institutional Development Plan

for

*evaluation and classification for certification
of organizations and institutions from
the research and development national system*

2011, December

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Introduction

This is the **Institutional Development Plan** of *Institutul National de Cercetare – Dezvoltare Chimico – Farmaceutica* (National Institute for Chemical Pharmaceutical Research and Development) – *INCDCF-ICCF* realized in the context of the institutional evaluation process required for Romanian research units or institutions to gain access to public institutional research funds¹. The report addresses the period 2007-2011. For INCD - ICCF the process has been initiated (officially) – and will be coordinated - by the Consultative Council for Research Development and Innovation at the request of National Authority for Scientific Research (ANCS) on 16/17.11.2011.

The structure of this institutional development plan has been established by law².

The development plan starts with a presentation of a scientific SWOT analysis made in order to find the strengths and weaknesses of our teams and to identify proper opportunities and potential threats that could affect from scientific point of view the institute scientific activities. By using the conclusions of this scientific analysis **the strategic scientific objectives** and **research directions** will be established for the next 4 years.

In order to reach these objectives the institute need some specific investments in human resource (and we presented also a **strategy for the development of human resource** and recruitment actions) and in infrastructure (for that a strategy was drawn and an **investment plan** proposed).

To maintain the scientific interest of our institute at the highest and new tendencies of international science levels we present some **instruments and mechanism** that will be used during 2012-2015 for supporting the **appearance in our research teams** of new scientific directions.

To support all these main targets we need financial support so we prepared a **financial SWOT analysis** to understand our potential and to define actions to improve weaknesses by using the existing (and next) opportunities and face to threats from financial point of view.

The report concludes with 2 very important sections namely specific actions for supporting the **technology transfer and attract non-public funds** and also the creation of new (**strategic**) **partnerships** for new cooperation projects, participate at specific events and activities related to RDI and increase our institute **visibility** at both national and international level.

1. Scientific SWOT Analysis

Strengths of institute from scientific point of view

- High-skilled and experienced key-staff with diverse backgrounds (53 researchers with diverse background education and expertise - chemists and chemical engineers, biochemists, microbiologists, physicians, experienced in bio- and chemical synthesis, microbial and extractive biotechnologies, analytical chemistry, pharmacology) capable to accomplish a multi-disciplinary research project.
- The research departments and teams suitable structured, assuring the keeping of the core competence claimed in the institute's mission.
- Good share or attested researchers into the total staff of institute (48%), good representativeness of PhDs and PhD students (21 respectively 10 out of 63 attested researchers)
- Existence of technical staff devoted to research teams (19 persons as auxiliary technical staff of 88 persons dedicated to RD activities – 22%)
- Modern infrastructure, especially for analytical and pharmacological characterization of compounds and formulations.

¹ Government Decision 1062/19.11.2011

² *ibidem*

- Pilot facilities (partially modernized) with their own utilities sources, allowing product development activities and ISO-certified small-scale production.
- GLP certified laboratories, with specific quality management systems, able to perform contract research activities and other qualified services.
- Active R&D partnership with research and education organizations (universities, other RD institutes, private sector).
- An existing innovation portfolio (patents and know-how).
- Effort made by the managerial team to support the personnel to improve technical and scientific skills (PhD, PhD students, postdoctoral, scholarships – 7 PhD student thesis)
- Application of a leadership based management and not a control-based one, decision-making processes and responsibilities being largely distributed to the sub-units (departments).
- Collective consultations and unity of the top-management in implementation of their main decisions.
- Large consultations and autonomy of researchers in project proposal initiatives.

Weaknesses of institute from scientific point of view

- The strategic objectives of the previous institute strategy were not enough measurable, realistic and timely.
- The shortage of national public research funds led to some funding-oriented topics, deviating from the main objectives and directions of activity, specific to the claimed core competence (in the economic crisis context).
- Lack of some high-tech infrastructure necessary in drug discovery, biotechnology and formulation: high throughput screening, genetic engineering and bioengineering, nano-pharmaceuticals.
- Relatively low presence (visibility) in the main worldwide (ISI indexed) scientific journals due to the old, traditional organization's culture, oriented mostly to applied research resulting in patents or industrial know how, a long-term absence of modern infrastructure followed by the shortage of research funds.
- Low level of funding by R&D&I contracts with industrial partners.
- Few international partnership and cooperation.
- Absence of outside scientific or stockholder representatives in the Scientific council and/or in an Advisory group. Their presence was provided by the previous strategy, but neglected by the top management
- Low number of middle-aged researchers to train the young ones.
- Staff aging – need for young people
- Lack of funds allowing international patent applications.
- Funds shortage led to incomplete exploitation of modern infrastructure.
- Few research people specialized in modern medicine formulations (e.g., nano-pharmaceuticals).
- Low level of salaries for scientific personnel
- Very low capacity of marketing the project results – real needs for improvement

Opportunities

- Lack of powerful competitors on the domestic market due to the specific core competence of the institute in pharmaceuticals.
- Present interest and future outlook for the R&D domain and topics on the European (e.g., EU-RTD Programs) and international level corresponding to the institute's mission.
- Existence of EU regional development funds for Romania, favoring to turn to account the institute's Knowledge and know-how in the economic environment.
- Presence in Romania of industrial producers and interested investors in the field of plant

extraction pharmaceuticals and/or nutraceuticals (possible partners).

- A recognized necessity in EU countries and worldwide of reconsidering the development of national industry on local favorable resources of raw materials and knowledge.
- Existence of funding (national and international) programs as instruments for implementation of national or international strategies / policies for health sector – the main sector of INCD – ICCF interest (National RDI Plan 2007-2013, Structural Funds 2007-2013, EU Strategy 2020, etc)
- Good opportunities to attract young people to research teams of INCD – ICCF by supporting their needs / training (scholarships, masters, PhD, post-doctoral) using the Structural Funds 2007–2013
- Reduced competitors on the domestic market on INCD-ICCF field of expertise

Threats

- Continuous shortage of national public research funds may lead to an irretrievable lagging behind the scientific progress in the field and loss of the core competence.
- Decrease of the domestic and EU market produced by EU crisis reducing the investments in new products and technologies.
- Few industrial partners limited to plant extraction pharmaceutical/nutraceutical producers leading to a customer pressing on and decreasing the institute's capacity to keep its full competences and to negotiate favorable contracts.
- Tendency of some local pharmaceutical producers to purchase foreign licenses of generic medicines reaching a poor level of therapeutic competitiveness, but enough to maintain a profit margin on the domestic market, instead of appealing R&D organizations.
- Reduced capacity for innovation of private Romanian companies
- Continuing of crisis – huge impact on RDI budgets (lower and lower) and activities/results
- Lack of private companies on our sector of activity interested on innovation and technology transfer
- Reduced number of researchers at national level and the brain drain of young people
- Bureaucracy – become a barriers in accessing public funds
- Reduced cooperation between universities, industry research centers
- Low involvement of government on RDI sector
- Fragmentation of the national RDI system

2. Strategic scientific objectives and directions

The main **priority objectives** of the institute are related to the major aims we consider to maintain and develop our organization:

- To prove a leading role in pharmaceutical R&D&I activities in Romania by maintaining and consolidating the core competence of medicines development.
- To become a reliable partner for international research co-operation partnerships and customers.

Obviously, reaching these aims means to strengthen the institute's position, starting from the scientific SWOT analysis.

2.1. Achieving and implementing public financed R&D&I projects, corresponding to the claimed mission of the institute

2.1.1. R&D&I (expected) projects financed from national public budget programs

Period, years	1	2	3	4
ICCF coordinator	2	2	5	5
Partner	7	7	16	9 ^{*3}

³*end of projects started in the 1st year

2.1.2. R&D&I and knowledge transfer (expected) projects financed from EU funds: RTD&I programs (e.g., FP7, Horizon 2020), from structural/regional development funds (e.g., cross border cooperation-knowledge transfer to the economic media and local authorities, economic competitiveness) and other international funds (e.g., NATO, Switzerland)

Period, years	1	2	3	4
ICCF coordinator	1	1	2	2
Partner	2	3	3	3

2.2. Increasing visibility by publications in international (ISI indexed, worldwide) journals or in books edited by well-known publishing houses

Period, years	1	2	3	4
Publications	25	35	45	55

2.3. Qualitative and value increase of R&D&I activities by partnership with industrial companies.

A change in structure of private funded activities is considered, compared to 2011, meaning more and valuable R&D&I projects, so that the value ratio of such projects to non-research services reaching 1:1.

The efforts should be oriented to attract interested international companies in common projects of product/technology development. Having in view the local and EU economic crisis, new market niches should be searched: non-EU, emerging economies (e.g., Russia and former SU-countries). By partnership agreements with such companies, 3 international patent applications should be submitted.

2.4. Creation of at least one innovation structure, possible a spin-off company, on the basis of innovative achievements of the team working in plant extraction R&D.

2.5. Scientific research directions

Aiming to achieve the strategic objectives, the scientific directions are based on two main principles:

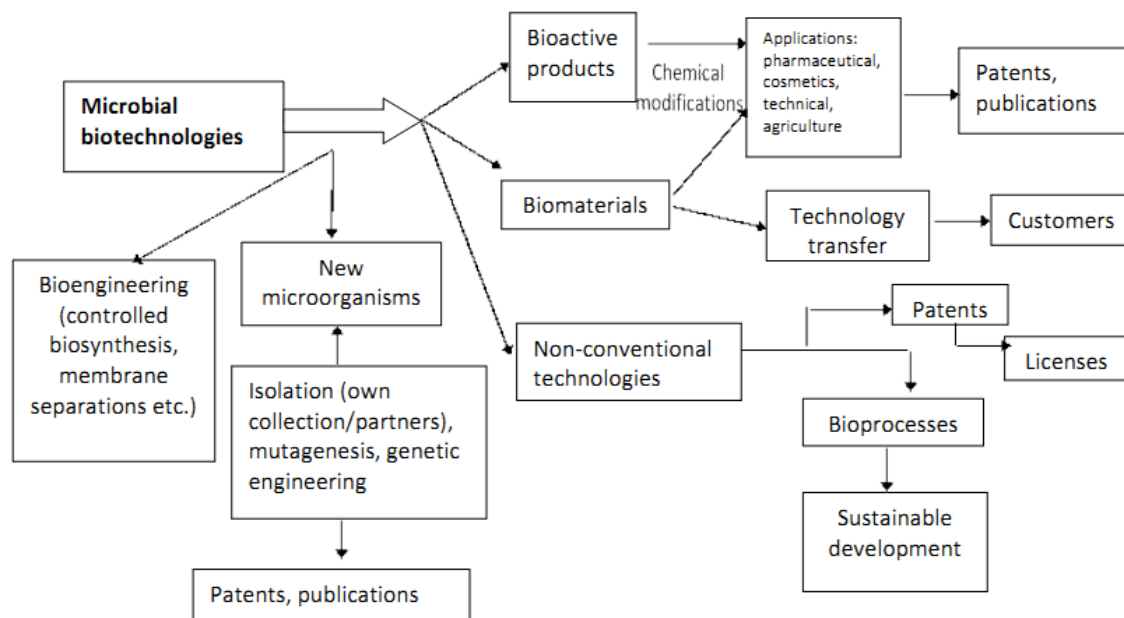
- to follow the actual trends in the fields of activity having in view those topics in which the institute has got a long term expertise and their qualitative improvement
- to develop innovative products and corresponding technologies which turn into good account renewable resources of Romania
- to consolidate the competitive advantage in some domains of large and actual interest (e.g., non-pharm bio-products: biopesticides, biofertilizers).

2.5.1. Biotechnologies

We aim to develop the two traditional directions of the institute's activity: microbial and extractive biotechnologies.

2.5.1.1. Microbial biotechnologies

The following scheme is considered to be relevant to our R&D activity in this direction and our view on results turning to good account.



Timing: Years 1-2

- Isolation and screening of new microbial products

The institute has a **collection of industrial microorganisms for about 40 years**, affiliated to the World Federation of Culture Collections (ICCF-22). New microorganisms have just entered the collection (from partners and exploration in extreme environments-polar, desert).

New bioproducts are expected to be found by classical separation procedures and their biological activities and other useful properties to be checked internal (enzymes, antimicrobials, biopolymers) or in partnership (antiviral, anti-tumoral). They could be identified as classes of compounds in the institute and as structure by partnership with specialized research/education organisations (organic/polymer chemistry), as well as their producing microorganisms.

Mutagenesis studies to improve the producing potential (physical treatments-irradiation by outsourcing) are also considered.

- Biotransformations

Known enzyme (e.g., lipase) producing microorganisms will be cultivated, their fermentation products tested in chemical synthesis reactions (see below).

- Bioengineering

In this period, only pilot fermentation experiments and isolation for microbial prepares from already known microorganisms dedicated to agricultural and/technical applications are considered, excepting other international project proposals.

Timing: Years 3-4

- Bioengineering-fermentation, isolation, purification and characterization of the new bioproducts for enlarged application tests and chemical modification.

Bioengineering studies to elaborate optimized biotechnologies of the perspective bioproducts obtained in the previous period. The purified compounds will be passed to enlarged pharmacological and application tests, including partnerships.

Some compounds will be passed to chemical synthesis researchers to perform chemical modifications for obtaining superior pharmacological/other useful properties

-Introducing genetic engineering techniques to obtain high-producing microorganisms (recombinant)

2.5.1.2. Extractive biotechnologies

The institute has a long time tradition and results in this direction, since its founding. It is a very actual research direction. In the last years, 61% of the new drugs have a plant origin. For Romania, taking into account the high diversity and richness of flora, as well as the relatively low

level of pollution, foreign experts consider this domain a very promising and capable to find a niche sector on the pharmaceutical world market. Therefore, this direction has been kept as priority in our R&D activities.

The following scheme tries to be suggestive for our planned activities in the field.

Some advantages of such products are a general lower toxicity, compared to synthetic structures, the possibility to start as food supplement and meanwhile to develop a medicine.

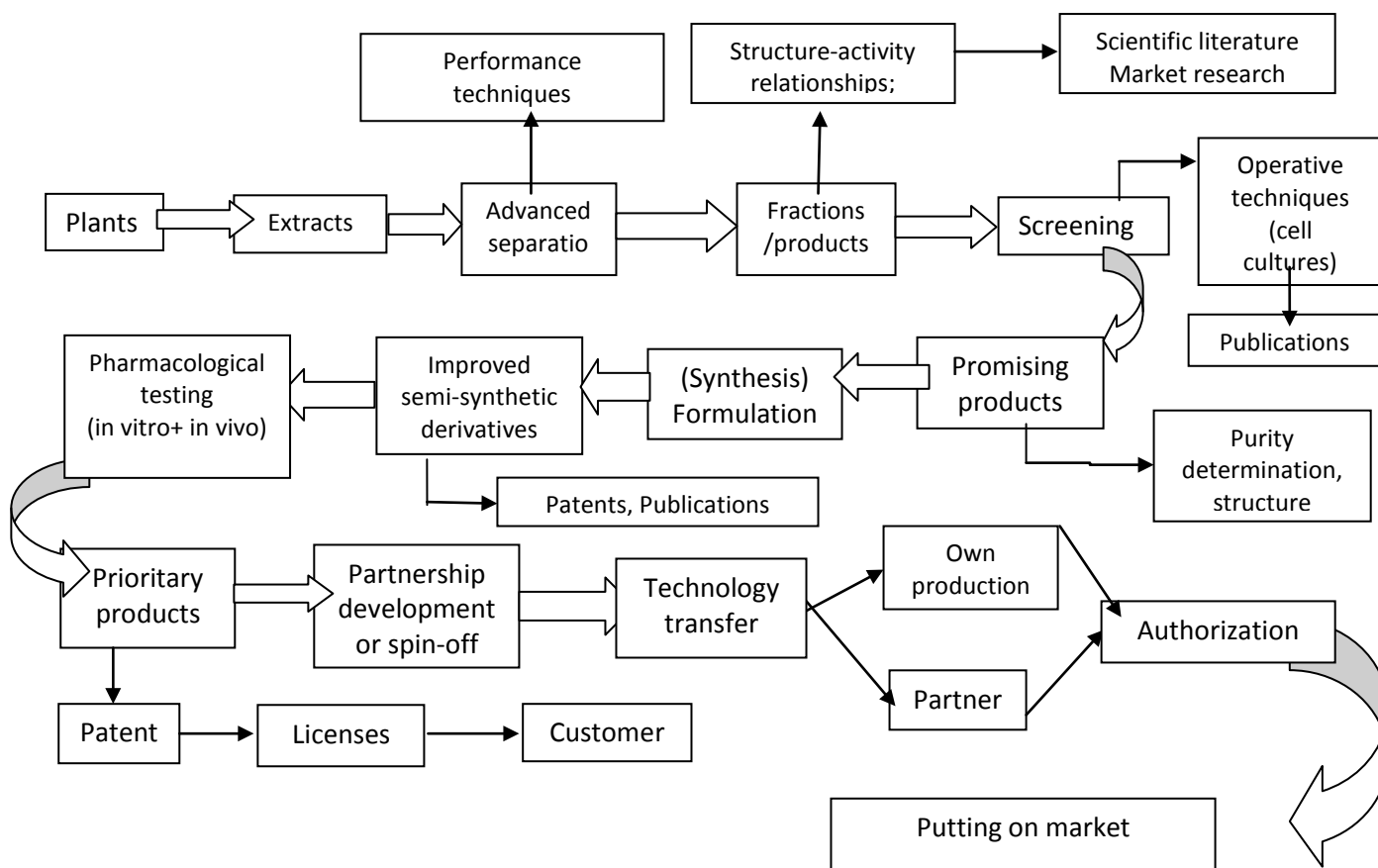
Timing: Years 1-2

- Going on with value-added products as selective fractions (concentrates) single or combined on active principles effect basis (a drug-design type, starting from the known bioactivity of active compounds and selecting the plants accordingly)
- Developing well characterized and standardized extracts for Romanian plant extraction pharmaceuticals/nutraceutical producers, in relation with interested farmers.

Timing: Years 3-4

- Isolation of advanced separation (UF, RO) fractions or single compounds (prep. HPLC, Centrifugal Partition Chromatography) for specific pharmacological tests.
- Pilot obtaining of perspective compounds to be passed to synthesis of improved semi-synthetic derivatives (as specific activity and/or pharmacology).

The following scheme tries to be suggestive for our planned activities in the field.

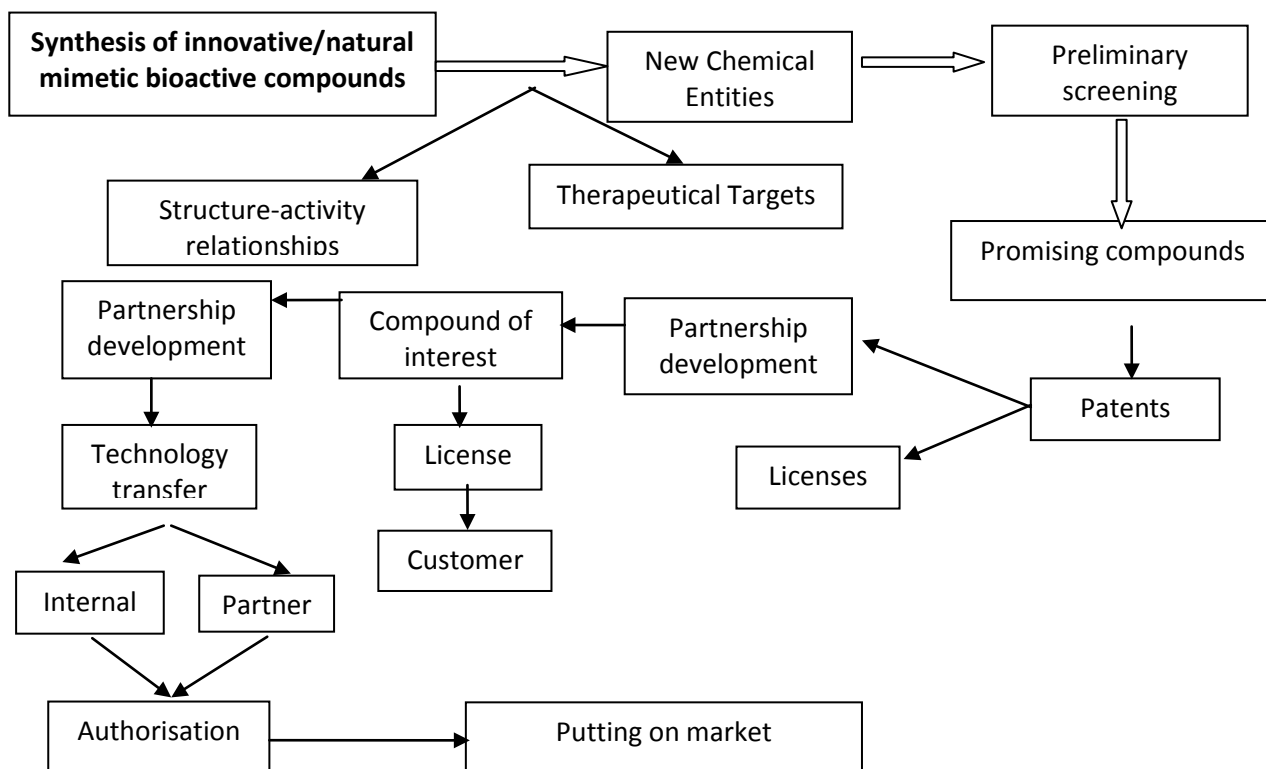


2.5.2. Chemical synthesis of bioactive compounds

In this R&D activity we maintain two main directions: innovative compounds and generics technologies.

2.5.2.1. Innovative drug substances

Our vision on this kind of research is presented in the following scheme.



From the “promising compounds” step, a partnership with a powerful partner company is essential for the future development

Years 1-2

- Ongoing research for new potentially therapeutic compounds dedicated to therapeutic major demands, e.g. anti infectious (antiviral, antimicrobial), anti-tumoral, selected by structure activity relationships. (SAR, QSAR).
- Introducing white (green) chemistry procedures using enzymatic reactions in different media, environmental friendly (e.g. ionic liquids, supercritical CO₂).

Years 3-4

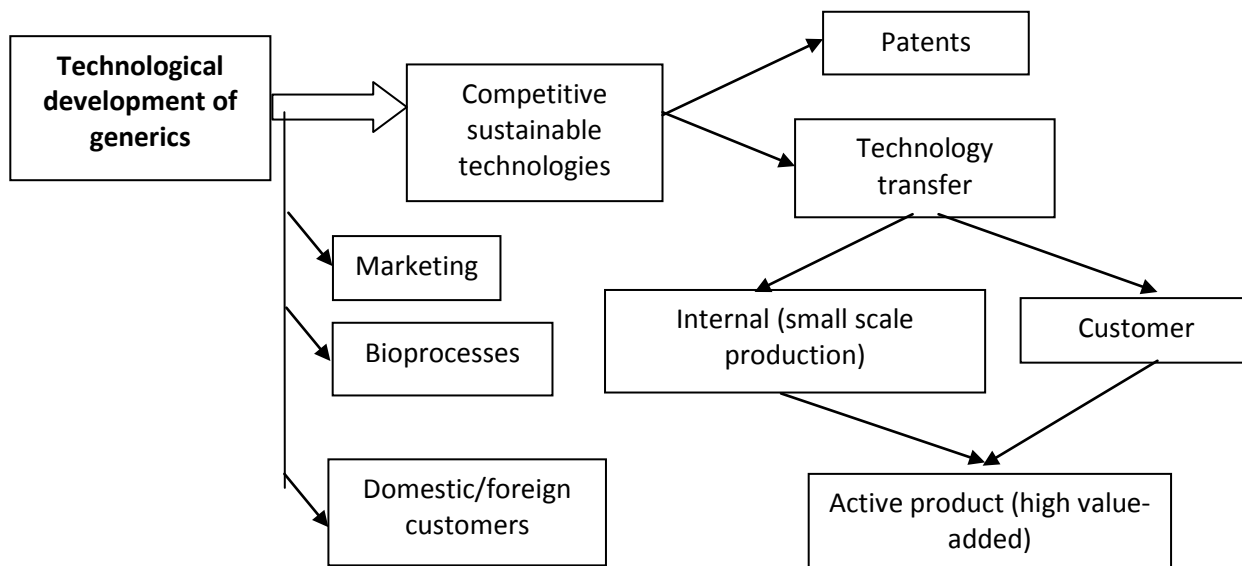
- Developing computational drug-design techniques by ligand-based drug design and virtual library design
- Selecting promising compounds from high therapeutic screening results (see pharmacological research) and elaborating their synthesis technology.
- Synthesis of semi-synthetic derivate starting from the biotechnology products

2.5.2.2. Improved technologies of generics

Heaving in view previous successful results in turning to good account such technologies on the foreign market, as well as the outlook of redeveloping in Europe the active pharmaceutical ingredients industry oriented to complex, high-value added compounds, we consider necessary to continue such oriented R&D activity following the scheme presented further down.

The following principles will be continuously kept in mind:

- Introducing white (green) chemistry procedures (biotransformations)
- Stereoselective catalysis(bio/biomimetic catalysis) to obtain valuable chiral compounds



2.5.3. Pharmaceutical technologies

As the number of new medicines (containing new active molecules) are decreasing, because of the several requirements especially regarding safety, involving increasing costs, difficult to afford even by big pharma, more and more attention is paid to new formulations with superior biodisponibility and higher safety.

In these topics, micro and nano-particles formulations, controlled release, target oriented and capable to cross biological barriers are prioritaire.

Our team started with liposome formulations of antimicrobials, enzymatic and hormones, with good results (non-published yet).

Timing:

Years 1-2

- Magnetic biopolymer coated nanoparticle formulations for blood clot preventing and destroying (with anti-thrombotic agents) targeted to coronary arteries obstruction in heart infarct.
- Liposome formulations of natural plant extraction, antioxidant and anti-tumoral compounds as preventing and adjuvant agents in cancer

Years 3-4

- Nanoparticle target formulations with block copolymers (starting from our developed biopolymers) containing anti-tumoral agents.

2.5.4. Analytical (physico-chemical) research

It plays a major role in evaluation of any preparative research result. Having a GLP from the National Medicines and Medical Devices Agency and ISO 17025 certificates, this laboratory performs EU recognized studies.

The specific activity is oriented to characterize new active compounds, adjuvants and formulated medicines, as well as packaging materials according EU and international requirements

The main R&D ongoing activities will continue:

- Elaboration of validated methods to identify and determine the chemical composition of new complex bio-products.
- Checking structural characteristics and purity of new synthetic compounds.
- Determine the presence and content of toxic impurities according EU and international norms (e.g. Pharmacopoeias)
- Stability and in vitro biodisponibility studies of the institute and partners/customers products.
- Elaboration of the pharmaceutical data section as component of CTD-Quality (Common Technical Document) for medicine approval.

Fine structure determinations are not possible now in the institute and are performed by partners. They are planned in the next future (years 1-2) by introducing of a GC-MS system and in the 4th year by introducing NMR.

2.5.5. Pharmacological research

The aim is to perform the preclinical (non clinical) characterization of the new pharmaceutical and similar products. This includes the determination of specific biological activity and toxicology, in vitro and in vivo. Regarding the specific activity, a microbiology laboratory (GPL) performs antimicrobial studies, other activity studies, as well as toxicology are performed in the cell culture laboratory and in the biobase (modern equipped), excepting anti-viral and antitumoral ones, carried out by partnership.

Years 1-2

- Extending the application of alternative (in vitro) system for organ-specific toxicity evaluation (neuro-, immuno-, hepatic), genotoxicity, teratogenic, local tolerance.

Years 3-4

- Introducing high throughput screening methods on molecular, cellular and organ-mimetic structures.
- Biomarkers identification and ligand–cell receptor studies

Note regarding the role we consider useful to be played by the National Authority for research.

Keeping in mind:

- The recognized importance for every EU country of the pharmaceutical sector and its industry (whose R&D is considered the “blood”) not only from the direct economical point of view, but for the quality of health and consequently quality of life, directly influencing national health expenditures (available good quality medicines means decreasing of hospitalization and sick leave expenses) and indirectly the people’s capacity of work;
- The importance given to medicines research by the EU-RTD programs (e.g. the Innovative Medicines Initiative), we consider necessary a proposal of a national research program in the field bringing together the Romanian R&D organizations, industrial stakeholders, national health authorities.

Other problems to be solved on a higher level than of a single organization:

- To renew at ANCS the discussion and making a decision on founding in Romania an International Depository Authority of patented microorganisms (like in the neighbor countries) essentially needful to patent microbial biotechnologies involving innovative microorganisms.
- Direct support (subvention) for expensive equipments purchase (e.g. NMR spectrometer, genetic engineering, high throughput screening equipment)-see capital investment plan.

3. The human resources strategy

The following **objectives** are established for the development of the human resources in the next 4 years:

1. **Quality of resources** – requirements for the research personnel:
 - high level of knowledge and professional competence
 - initiative and capacity of independent work
 - team spirit and communication abilities
 - flexibility in project approach and development
 - a research and performance culture, career development
2. **Stability and growing younger proportion**

3. Structure according to the priority scientific directions

Principles and actions to reach the objectives

Recruitment. For young graduate people, it starts even during the university studies, attracting those students showing qualities and desire to work in research.

There are several ways we have noticed as successful:

1. Selection by our staff performing teaching activity
2. Recommendation of teaching people from the partner education organizations
3. Attracting young people by the practice terms carried out in the institute and by our website
4. As employing criteria, the CV content, graduation marks, previous scientific work, communication and foreign language abilities are also considered.
5. The young graduates should be in course or passed out a post-graduate or PhD stage.

Our personnel needs belong especially to chemical synthesis, plant extraction, modern formulations and pharmacology (chemical engineering, chemists, pharmacists, biochemists). Their number will depend on the kind of financed projects.

To cover the lack of specialized personnel in critical priority directions (e.g., computational drug design, nano-pharmaceutics, plant extraction, commercial exploitation of R&D results) we have started to employ specialized research/education staff on part-time working, preferring young PhD or PhD students. We intend to make efforts attracting young PhDs which performed traineeships abroad.

Stimulation of increasing professional level. Traineeships, mobility.

Outside training

- PhD and post-graduate students – adapting the working schedule, sponsoring their PhD taxes, conditioned by an obligation to remain working in the institute 2-4 years. Decreasing by retirement from 2007 to 2009 (22 to 16), the number of PhDs (from our PhD students) has increased to 21 at present and is expecting to further increase, having in view the existence of 10 PhD students now.
- Some PhD and PhD students have performed traineeships in prestigious foreign education/research organizations, financed from EU programs (e.g., POSDRU), or in the frame of bilateral cooperation projects of the institute – e.g., in France-Paris-Sud 11 University-Faculty of Pharmacy (drug design), Hungary – Biological Research Center of Szeged (molecular biology), Budapest University of Technology and Economics – Applied Biotechnology and Food Science (microbial biotech), as well as in Romanian universities.

We intend to extend these activities by traineeships in other foreign institutions being in partnership relations (informal or preparing RTD EU project proposals) – e.g., Technical University of Munich, Lisbon University (biopolymers), as well as in departments of excellence from Romanian partner organizations: e.g., Cantacuzino Institute (microbiology), Institute of Virology, Institute of Cell Biology and Pathology (cell and molecular biology). A modern way is attending webcasts.

Internal training. By team structure (experienced and young people), roundtables.

Stimulation of initiative and capacity of independent working

Every research person (not depending on the research degree) could make research project proposals, manage specific activities or even internal research projects or laboratories.

Flexibility in project approach and development – accomplished by the large range of backgrounds (chemists, biochemists, chemical engineers, bioengineers, biologists, physicians, pharmacists).

Team spirit and communication. The multi-disciplinary specific of research favors inter-departmental team structures with long-term communication usage, but “not every group make a team” and we should pay attention especially to young colleagues integration. Modern forms to evaluate the adequacy of the team composition will be introduced (e.g., anonymous evaluation questionnaires from the colleagues).

Research and performance culture, career development.

Motivation. The collective labor contract clearly provided salary awards for recognized excellence of research results (publications, patents, special results in technology transfer) as well as a salary level depending on work and performance in R&D projects and attracting non-public funds. This last principle has been respected, but the awards have been unfortunately sporadic, because of the permanent financial crisis.

Limited by the financial difficulties, justified participation of researchers to scientific or promotion meetings has been supported. In spite of such constraints, promotion of research personnel to superior research degrees has permanently encouraged and corresponding competitions have been organized.

Ethics. Special attention has been paid especially by the Scientific council, to promote the professional ethics, as it was provided by the Romanian Law no. 206/2004 (modified and completed by the Law no. 398/2006, Gov. Decision no. 28/2011) and the European Commission Recommendation C(2005)576/11.03.2005 containing the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers. A member of the Scientific council was appointed to monitor and organize specific activities on these topics, preventing and correcting non-ethics practices.

Gender issues. The research personnel has been mostly of feminine gender and this proportion is well-reflected in the composition of management structures.

Stability and growing younger proportion. The proportion of R&D high-educated people aged under 45 years has increased from 25.4% in 2007 to 34.5% at present, with less than 10% fluctuation. We want to increase it to 40-45%.

4. Mechanisms for stimulating the appearance of the new research directions

Such mechanisms have been created in the institute to provide a permanent flow of generation and selection new research ideas. They are based on two basic principles, part of the culture of our organization: a) our R&D activity is part of the whole efforts on national, EU and international level; b) partner and customer oriented attitude.

Thus, one mechanism of stimulating the appearance of new research topics is to start from national strategies in the related fields (biotechnology, health, agriculture, environment) and from the EU-R&D strategies and RTD Programs topics, as well as from the worldwide recognized published foresights, overview and outlook monographies on drug discovery and medicines development or on related topics (e.g., bioresearch).

Studying the EU priorities, we shall network with education/research institutes from EU countries, submitting together proposals and being part of the EU research contribution to industrial competitiveness and scientific progress.

More attention will be paid to priorities of non-EU countries too, and to elaborate our own forecast scenarios.

On the national level, the programs financed from the Structural EU Cohesion and Regional Development funds, whose projects we have been already involved in (administrative capacity–marketing and promotion, economic competitiveness with a SME, RO-BG cross-border cooperation) are a good opportunity of knowledge transfer to local communities, but also to build up a permanent dialog with local administration and business communities and thus to set up new topics.

The other mechanism starts from our education/research partners ideas, directly presented or by our PhD students, setting together their PhD thesis topics, or from private research or production companies. For example, our activity topics in nanopharmaceuticals have been suggested by the Pharmaserv International Ltd. Company from Romania. By research services performed for industrial producers, they are also informing us on their perspective needs related to new products. An important event in this way was also our active participation at the Caravan of Innovation organized by ANCS in 2008 through all of the 8 development regions of Romania, setting up a communication line to assess the requests and suggestions of the industrial and business environment.

We have the use to organize or to be part of debates on our topics with other partners and ANCS officials. We also try to apply “competitive intelligence” in maintaining our competitive advantages in some areas (e.g., microbial and extractive biotech).

For customer-oriented R&D topics we also intend to be connected to international market demands (e.g. NineSigma innovation network).

The mechanisms of stimulating new ideas for research directions work from two directions: top down and bottom up. Thus, it is possible to have a drive represented by the institute's strategy and to have staff permanently involved in this digging in process. Everyone's proposal is accepted in debates, assessed as priority and performing possibilities and a collective decision is made, firstly in the Scientific council, secondly approved by the Executive committee and top managers. The project proposals are entirely transparent and their accomplishment after passing a competition is collective monitored.

Generally, we will try to keep a balance between maintaining a short term competitiveness and long term exploratory research. We also try to give to researchers, as possible, some autonomy to propose and check some research ideas by themselves, free from a formal plan.

5. Financial SWOT analysis

Strengths of our institute from financial point of view

- good capacity to attract financial sources for RDI activities through funding programs
- possibility for renting spaces unused for the RD activity to various clients (new incomes)
- existence of a portfolio of patents and know-how suitable to be develop and/or transferred to the business environment
- modern infrastructure for partnership in RDI, specific services and small scale production

Weaknesses of our institute from financial point of view

- low level of researchers salaries;
- low schemes of bonus used to motivate the research staff according to their performances (from financial point of view)
- reduced incomes from national public sources – decrease by 34% in 2011 compared with 2007, determined by the financial negative impact of the economic crisis (lack of calls for proposals, budget reduction for RDI, budget cuts of the contracted projects)
- low capacity to attract private financial sources/incomes
- low financial potential to acquire new and high performance equipment;
- low capacity to finance travel abroad (at the level of the real need)

Opportunities

- National and international funds available for RDI - financing opportunities for our sectors of expertise (Biotechnologies, agriculture, health, environment);
- Renting available spaces not used for RDI activities;
- Higher disponsibility of universities to R&D partnership

Threats

- Reduced budget for RDI in 2012 state budget project
- Reduced interest of government for health and agriculture – our main sectors of interest for RDI activities (unsatisfactory budgets, inefficient policies of personal – salaries, financial – fiscal, reduced support to increase SMEs participation at RDI activities – proper incentives)
- Brain drain (young persons are leaving the RDI sector as it is an unsafe and unattractive sector do to the low RD financing);
- Reduced level in the last years of Foreign Direct Investments in Romania
- Long term reimbursement of expenses from the EU structural funds projects could be determine temporary disorders in cash flow leading to lack of financial liquidity
- Lack of constantly organized R&D competitions from national public funds leading to an underfinanced activity.

6. Infrastructure: investment plan and strategy

The investment strategy for infrastructure development and its corresponding plan represent a major condition of the quality of R&D results. The investment funding has been composed by a subvention from the public budget, attracted funds from R&D public financed programs and our own sources (annual depreciation fund and extra-public budget income).

During the last four years, the public subvention was oriented partly to modernize the pharmacology building according to EU requirements, having in view the necessity of reliable and recognized results, not only for our R&D projects, but for contract research services and assays ordered by partners and clients. Another part of the subvention funds was dedicated to rehabilitation investments and a necessary pre-epuration plant needful to continue a normal, safe activity and to obtain an environment certification according EU requirements. Thus, the used heating devices and pipelines, as well as the electric main switchboards were changed, a thermal rehabilitation of the buildings has just started (all of these rehabilitation capital investments were positive assessed as energy saving).

The attracted funds from R&D projects were almost entirely not from proper R&D projects (whose financing has been drastically cut since 2008), but from R&D infrastructure development dedicated programs (R&D capacities).

Thus, modern equipment was purchased for analytical laboratories (e.g. ULTRA-PLC-MS, HPLC-MS-MS, ICP-MS systems), biopharmacology (e.g. flow cytometer) and a pilot plant for biotransformation, fine synthesis, extraction and purification of active ingredients. This plant, apart of scaling-up processes, has been considered useful to obtain necessary product quantities for chemical trials and to be involved in a future spin-off or partnership production for extractive biotechnologies.

The plan of future investments follows the proposed technical scientific directions achievements and their time schedule as well as other envisaged future developments.

We will also keep in mind to assure a suitable training of the R&D personnel adjusting their qualifications to the equipment qualifications.

Direction	Main necessary infrastructure	Estimated value EUR
Microbial biotechnology		
1-2 years	MALDI Biotyper (MS-microorganisms identification)	160.000
	Computer controlled:	
	Mini-bioreactor system	100.000
	Microfermenter 30 l (bioengineering)	100.000
3-4 years	Pilot bioreactor 80 l	120.000
	PCR/RT-PCR, DNA sequencing, electroporator, DNA/RNA synthesizer	450.000
Extractive biotechnologies		
1-2 years	Pilot formulation line (capsules, syrups)	110.000
3-4 years	Laboratory CO ₂ supercritical extraction equipment	40.000
	Reverse osmosis module (advanced separation)	80.000
Chemical synthesis		
1-4 years	Multipurpose lab/minipilot systems (synthesis and separation)	200.000
Pharmaceutical technologies		
1-2 years	Particle size analyzer	80.000
3-4 years	Ultracentrifuge (nanopharmaceutics)	80.000
Analytical (physico-chemical) research		
1-2 years	GC-MS-MS system (biopolymer structure)	90.000
3-4 years	NMR 500-600 H ₂ (fine structural analysis)	600.000
Pharmacological research + Biotechnologies + Chemical Synthesis		

1-2 years	Histopathology system (for in vivo pharmacotoxicology)	140.000
3-4 years	Modular high throughput screening system	1.000.000
Software		
Predictive (in silico) modules	QSAR (multicase type) ADMET modular docking	200.000

This plan is ambitious, but essential to reach a competitive level on international scientific world. Obviously, it could be achieved only by a concerted effort of public budget funds (national and EU) for infrastructure development, equipment allocation from attracted R&D projects and our own extra-public budget contracts.

7. Technology transfer and the attraction of non-public funds

7.1. Technology transfer

We consider three directions of technology transfer:

- Spin-off/start-up company
- Transfer to an industrial partner/license transfer/partnership in production
- Internal transfer-small scale production, services

A spin-off company set up on extractive plant biotechnologies has been kept in mind during the last 3 years, taking into account the 6 patents and 10 patent applications of the team, as well as the good perspective of this sector. Such innovative company would develop products based on their own patents, the institute being the patent holder and participating with its laboratories and pilot plant. The interruption of the national innovation program and the 10% advanced expenses requested from the shareholders by the EU structural funds financing have been on obstacles not overcome yet and more difficult during this time of crisis, affecting creditation. We hope to step forward by the end of the 4 years term.

4 new products technologies (patented) were transferred to a plant extraction industrial producer (GMP certified) as national R&D project beneficiary, in 2006 and 2008 (3 in 2006, 1 in 2008).

There were 3 nutraceuticals (for respiratory viral infections, skin diseases, a sedative, antispasmodic) and one medicine (anticolitis). It is difficult to expect more such transfers in the next future, having in view the economic crisis, even no affecting so much the pharmaceutical industry, but we hope to maintain this level (4) in the next 4 years, mostly by the end of these period.

We intend to start license transfer and collaborative production activity with start-up SMEs. One such partnership in production of a plant extraction anti-stress ulcer pharmaceutical is planned in the next 2 years. The institute's extraction step technology will be taken over by the SME on the plant cultivation site and the product formulation in the institute pilot plant (see investments plan). At least other two products technologies will be transferred in the same way (one product on eye drops medicine will enter the clinical trials next year).

The internal transfer has been developed mostly in the period 2001-2007, resulting in an export to Italy of fine synthesis products (prostaglandins) reaching a maximum of approx. 150.000 EUR/year, but constantly decreasing since then because of the economic crisis and the dependence on a single customer.

Internal transfer of methods led to a diversification of analytical and pharmacological offer of research and other scientific services (see below).

7.2. Attraction of non-public funds

The attraction of non-public funds has been permanently aimed. Private financing has been obtained for research, specific services, and our own small scale production.

R&D financing from private sources reached a maximum in 2010 of approx. 200.000 EUR, from which 70% represented national clients. The R&D activities for domestic partners consist mainly of analytical and pharmacological studies performed on new products of Romanian pharmaceutical producers, but also for a complete R&D of a new pharmaceutical (one eye drops medicine from desert truffles), initiated by a Romanian business man from Syria. The product and technology were claimed in a Romanian and international patent applications. The product is now in pilot development and production of eye drops solution.

First series has been formulated by a Romanian pharmaceutical company, the preclinical studies have been very promising (eye infections, healing and glaucoma treatment in animals) and first clinical trials are expected soon. Having in view the future elaboration of documentation for putting on market authorization, future partnership in production and technical assistance in a new plant, a long term partnership is expected.

International R&D financing has been represented mostly by contract research for the same Italian client company for small scale fine synthesis products (prostaglandins).

It has drastically decreased since 2009 because of economic crisis and a necessary diversification of contract research offer and its promotions has become essential.

Specific services. They are represented by special analytical and pharmacological assays applying about 400 methods, performed responding to client demands. The clients are Romanian pharmaceutical producers, pharmaceutical companies from non-EU countries (e.g. Egypt, Gulf Emirates) by their Romanian representatives. There are approx. 65 such clients and the market was about 90.000 EUR in 2010. Obviously, it depends on their sales, but this market is expecting to be kept or even to grow, having in view the increasing quality requirements, especially for nutraceuticals.

As marketing research is made by the entrusted people, senior people are contacting suitable partners specialists. We also use to promote our offers and set up contacts by centers of technological information, regional development foundations.

8. Strategic Partnerships and visibility: events, communications, collaborations

8.1. Strategic partnership

We have in view both directions of strategic partnerships: on strategic sectors and with strategic partners. Regarding strategic sectors, we continue to maintain and to consolidate our project partnerships with national well-known universities, like those of Bucharest, Iasi (of medicine and pharmacy, basic and technical sciences). A lower level of collaboration has been yet developed with the Transilvanian universities (Cluj, Timisoara) and we want to set up more partnership relations in that area.

Other strategic sector includes specialized complementary organizations like research institutes or centers having excellence teams in chemistry (organic, polymers), cell and molecular biology, medical microbiology and virology, but also private companies (e.g. Pharmaserv International Ltd. Company).

Another direction concerns to strategic partners: we intend to consolidate previous and recent partnerships with renown universities and research centers, as well as with innovation companies (like Bayern Innovativ, Germany). Succeeding to interest a renowned innovative or big pharmaceutical company in one of our innovative compounds and setting up a strategic alliance to developing a new medicine remains a major goal.

8.2. Visibility

Since 1996, the institute has used to organize every 3-4 years its own scientific meeting with international participation (e.g. UK, USA, Germany, Israel, Hungary): "Drug research between information and life sciences". It was a symposium with several sections, according to the main scientific topics in the field. There were 300-400 participants/meeting from scientific and industry environment, a good occasion for visibility and starting partnerships. We intend to renew this initiative.

Because of financial constraints by cutting public research funds, our participation to scientific meetings abroad has been reduced. We intend to keep our presence at the main exhibitions of inventions and trade fairs. A deeper selection of the international scientific events will be made, preferring those which are regularly organized, with the participation of renowned personalities. The full publication of the communications in high-scored journals will be considered. A useful way of increasing visibility and setting partnerships we consider to be the attending of professional webcast.

