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100 Years *LONZA* – From a Product to a Market-Driven Enterprise

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Abstract. In recent decades, *Lonza* has transformed itself from a seller of 'what the plant made' to a producer of 'what the market wants', whatever the product, within the scope of our capabilities. This means that in addition to a constantly evolving list product gange *Lonza* now nurtures a corporate culture based on intimate relations with customer companies, which are often themselves industry leaders. This is particularly true in the life science industry where *Lonza* offers a combination of classical organic synthesis and biotechnology for the exclusive development and manufacture of advanced intermediates and active ingredients on a true partnership basis.

Shortly before entering the Simplon tunnel, the Paris-Geneva-Milan express train speeding up the Rhône valley passes alongside *Lonza*'s Visp works. Half an hour later, leaving the tunnel, the train, now no longer on Swiss but Italian territory, crosses the village of Varzo, the site of *Galtarossa*. Both companies – as a number of others built in Alpine valleys around the turn of the century – started their activity by producing calcium carbide from coal and chalk in electric furnaces using power from nearby hydroelectric power plants. But here the similarity between the two companies ends. Whereas *Galtarossa* ceased to exist in 1958, *Lonza* celebrates its centenary as a flourishing enterprise. How come this difference? There are, of course, a number of answers. Yet the prime reason for *Lonza*'s survival was its ability to anticipate, or at least adapt to new trends in the industry and in the business environment.

From a Local Smokestack, Supply-Push, Heavy Inorganic Chemical Industry...

If we try to track *Lonza*'s evolution with nitrogen as a common denominator (*Fig. 1*), we can vividely imagine the fundamental transformation that has taken place. *Lonza* started as a smokestack industry turning out low-added value inorganic chemicals from dedicated plants and selling them to nearby customers to become a differentiated producer of high-

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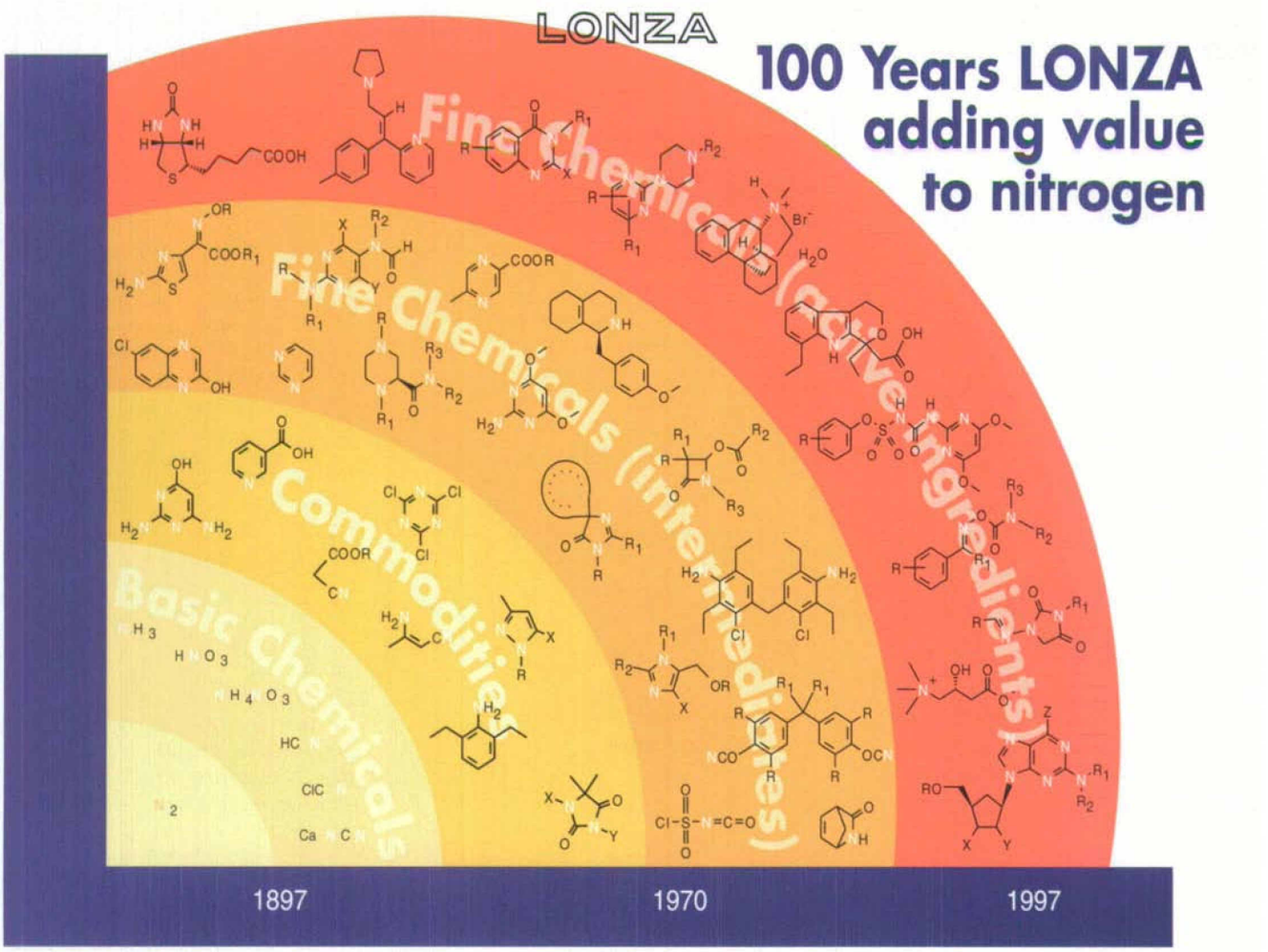

Fig. 1. LONZA – *100 years of nitrogen chemistry*

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added value fine chemicals in sophisticated multipurpose plants for the world's leading life science companies!

What at hindsight might look as a continuous evolution from nitrogen/calcium cyanamide to pyrimidines, purines, and other sophisticated N-heterocyclic compounds [1] in reality is a quantum leap between the opposite boundaries of chemical science (*Table 1*).

All in all, just about every facet of *Lonza*'s activities at the beginning and the end of the centenary has changed totally. In technical terms, one can reasonably assume that the only common denominator between the heavy inorganic chemical industry at the beginning and the fine chemical industry at the end of the 20th century is the cooling water which continues to flow as meltwater down from the Rhône glacier ...

Leaving aside the technical evolution from an electric furnace producing calcium carbide or calcium cyanamide to a multipurpose fine chemical plant, let us consider the main business aspects. Incidentally, the technical evolution illustrated in *Fig. 1* and *Table 1* has been paralleled by an equally dramatic evolution of the business condition.The milestones in the evolution of *Lonza* in these terms are reported in *Table 2*. The driving force at the beginning was a technical capability, namely operating an electrothermal process for calcium carbide, a product which could be produced largely from local resources and for which a local demand was expected. By expanding from the original product to calcium cyanamide, ammonia and fertilizer, a 'supply-push' strategy was unintentionally followed.

CaC_2, CaNCN, NH_3, NH_4NO_3 ⇒ local customers

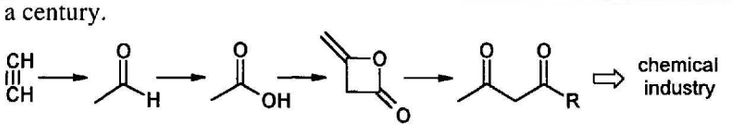
Driven by the sagging demand for calcium carbide, an in-house forward integration to acetylene had already been put into place during World War I. Production of the first acetylene-derived chemicals, acetaldehyde, acetic acid, and acetates followed suit. During World War II, the branch vinyl chloride monomer/PVC was added. In the fifties, on the wave of a rapidly expanding chemical industry, where capacity consistently lagged behind demand, this 'Stammbaum' (family tree) strategy, illustrated here with the 'diketene branch', proved to be successful for more than half a century.

Table 1. *Stretching the Limits of Chemistry*

	1897	1997
	technology	
raw materials	coal, lime	light virgin naphtha, natural gas
energy	electricity	steam from natural gas and waste solvents
plant	single-product electric furnace	multipurpose fine chemical
technology	licensed in from *Schuckert*	*Lonza*
	business	
customers supplier/customer interface	local farmers' cooperatives non	global life science industry partnership joint multidisciplinary teams
contract types	spot purchases	multiyear supply contracts
contract elements	quantity/price/delivery	quantity/price/delivery **plus** specifications, regulatory compliance, technology transfer, cost improvement, currency clause exclusivity, intellectual property rights, *etc.*

Table 2. Lonza *Business Milestones*

first half of the century	• shift from serving local end-user markets to supply of organic intermediates to the chemical industry • development of the 'Stammbaum-Chemie' (family-tree chemistry)	supply-push
60s	• shift from coal to petroleum as main raw material • establishing a position in the US by the acquisition of *BAIRD Chemicals* • establishment of commercial development • forward integration to ethylene oxide failed	
70s	• extending customer base internationally • International Sales Offices are established and English becomes dominant business language • beginning of exclusive business: 'Leave it to *Lonza*'	demand-pull
80s	• outsourcing becomes a business strategy of the leading life science company • Fine Chemicals Complex comes on-stream • exit from inorganics and PVC business	
90s	• broadening of the offering in fine chemicals: • biochemistry • bulk actives • product life extension • exclusive business becomes largest business of *Lonza Ltd.*	partnership
00s	• emergence of the virtual life science company • R & D becomes profit center • 50% of US fine chemicals sales are from local manufacture • biotechnology becomes major business	



R = OCH_3, OC_2H_5, NHAlkyl, NDialkyl, NHAryl

By the mid sixties, the 'foliage' of the *Lonza* family tree had become quite prolific, comprising dozens of organic intermediates ranging from methyl acetoacetate to barbituric acid, cyanuric chloride, malonates, pyridine bases, and nicotinic acid. The 'Big Four of Basel', *CIBA*, *Geigy*, *Hoffmann-La Roche*, and *Sandoz*, with their expanding agrochemical, pharmaceutical, dyestuff & pigment, flavor & fragrances, and vitamins divisions became *Lonza*'s major customers. The decision, in retrospect may be the strategically most significant one, was taken not to compete with customers. Thus, *Lonza* never ventured into the above-mentioned performance products. At hindsight, this decision appears to have gotten a confirmation by the recent strategic decisions of chemical giants to separate their life science from their purely chemical activities. Examples are *I.C.I./Zeneca*, *American Cyanamide/Cytec*, *MONSANTO/n.a.*, *Novartis/CIBA Specialty Chemicals*, and *SANDOZ/Clariant*.

At any rate, an impressive portfolio of organic intermediates today still constitutes one of the backbones of *Lonza*'s business.

In 1967, *Paul Walther*, a charismatic manager with extraordinary business and technical skills, was appointed to head of the newly formed Organic Chemicals Division. One of his first moves was to establish a commercial development function. This was in order to focus more systematically the further development of the product range. In order to promote new molecules found in R & D, which so far had been hold back as a company secret (!), a first Development Product List was published.

At the same time, two apparently unrelated events occurred. In an attempt to effectively use surplus ethylene produced by the cracker, a plant for ethylene oxide/ethylene glycol was built. It was orders of magnitude smaller than the plants of our competitors [2] and had to be shut down soon after start-up. At about the same time, *Chemical Abstracts* had listed its ten millionth molecule. Inventing compound 10000001 and hoping to find a market for it turned out to be a futile undertaking! Therefore, it became obvious, that in spite of the noble intention of 'cloning the imagination of chemists on molecules already manufactured', the first Development Product List marked the beginning of the end of the 'supply-push' strategy.

One of the early projects handled by Commercial Development, which also for the first time included a close cooperation between Research and Development and a commercial function, was the extension of the diketene branch of the family tree to include three groups of **γ-chloroacetoacetate** chemistry.

- First, an impressive list of *chloromethyl-pyrimidines* was developed, including an unsuccessful attempt to produce orotic acid by hydrolysis of 4-chloromethyluracil. Despite the assistance from *Battelle Geneva* in an attempt for commercialization, apart from a few university researchers (one pretended to have them successfully applied as antifouling agent for the paint of his sailing boat), nobody was interested in these fancy molecules, and the idea had to be abandoned.
- Second, a few existing 4-m^3 reactor vessels and a filter press, located in the so-called 'Zinsstag tower', were converted to a *quinacridone* plant. The five-fused-ring-membered, symmetrical quinacridone molecule is synthesized from aniline (or *o*-toluidine) and dimethyl succinylo succinate. The latter is accessible either by condensation of two molecules of methyl γ-chloroacetoacetate, or – how our competitors do it more economically – by the condensation of two molecules of dimethyl succinate.
- Third, ring closure of the γ-chloroacetoacetates with thiourea to substituted *2-aminothiazolyl-4-acetates* proved to be a successful undertaking. Upon further conversion to α-alkoximino derivatives, these compounds are produced still today in a number of variations as side chains for third-generation cephalosporin antibiotics, such as 'Ceftazidime' from *Glaxo-Wellcome*, 'Ceftiofur' from *Pharmacia-Upjohn*, 'Ceftriaxone' from *Roche*, and 'Cefpodoxime' from *Sankyo*.

...through a Strategy Turnaround ...

The success with the substituted aminothiazolyl-acetates triggered a transition from supply-push to demand-pull strategy. Commercial Development engaged in a systematic search of the patent and other scientific literature in order to identify more end products for which *Lonza* chemistry could be used to synthesize key building blocks.

For two reasons, this wide-angle search for new molecules, paralleled by a random search of our customers for suppliers of new molecules needed by their development sectors, had only a very limited success: *1*) Many more chemical structures are patented than actually developed – in many instances, our customers were not even aware of the structures we mentioned and for which we had developed a unique chemistry. *2*) Even when new drugs and agrochemicals belong to the same chemical class, they typically require entirely different synthetic approaches for an economic manufacture. Therefore, common building blocks for families of new drugs or agrochemicals are the exception rather than the rule. Examples are the modern *angiotensin II antagonists* which all exhibit an imidazole (or a similar space configuration) moiety (*Fig. 2*).

DuPont-Merck's 'Losartan', *Ciba-Geigy*'s 'Valsartan', *Sanofi*'s 'Ibesartan', and *SmithKline Beecham*'s 'Eprosartan', which are being launched in this sequence, all require different synthetic pathways for their industrial manufacture. The same applies to the blockbuster class of sulfonyl herbicides. Although most of them have the $-SO_2NHCONH-$ moiety in common, only a limited number are economically produced from *Lonza*'s chlorosulfonyl isocyanate.

In order to attract investors, the life science companies started publishing their new product pipelines. The reports of the financial analysts became an important source of information for us. It complemented the screening of patents and other scientific literature and allowed us to abandon the catch-as-catch-can business-development approach in favor of a more accurate analysis of the new pharmaceuticals and agrochemicals in development at our customers. Products were identified where there appeared to be a fit with *Lonza*'s capabilities and a discussion with the customers was sought.

new pharmaceuticals new agrochemicals

↓

tailor-made fine chemicals

Thanks to personal contacts on the senior managment level between *Lonza* and *CIBA*, the manufacture of **6-hydroxy-2-isopropyl-4-methylpyrimidine**, dubbed 'Promidine', the first exclusive product, was taken up at the end of the sixties. The deal already exhibited some of the characteristics of later successes:

- integration into family-tree chemistry: methyl acetoacetate, ammonia,
- integration of customer know-how,
- single-sourcing,
- highly successful customer product: 'Diazinon'.

Parallel to this, R & D undertook efforts to further develop the chemistry of major existing intermediates: with new processes for nicotinic acid and malononitrile, a world leadership position could be established.

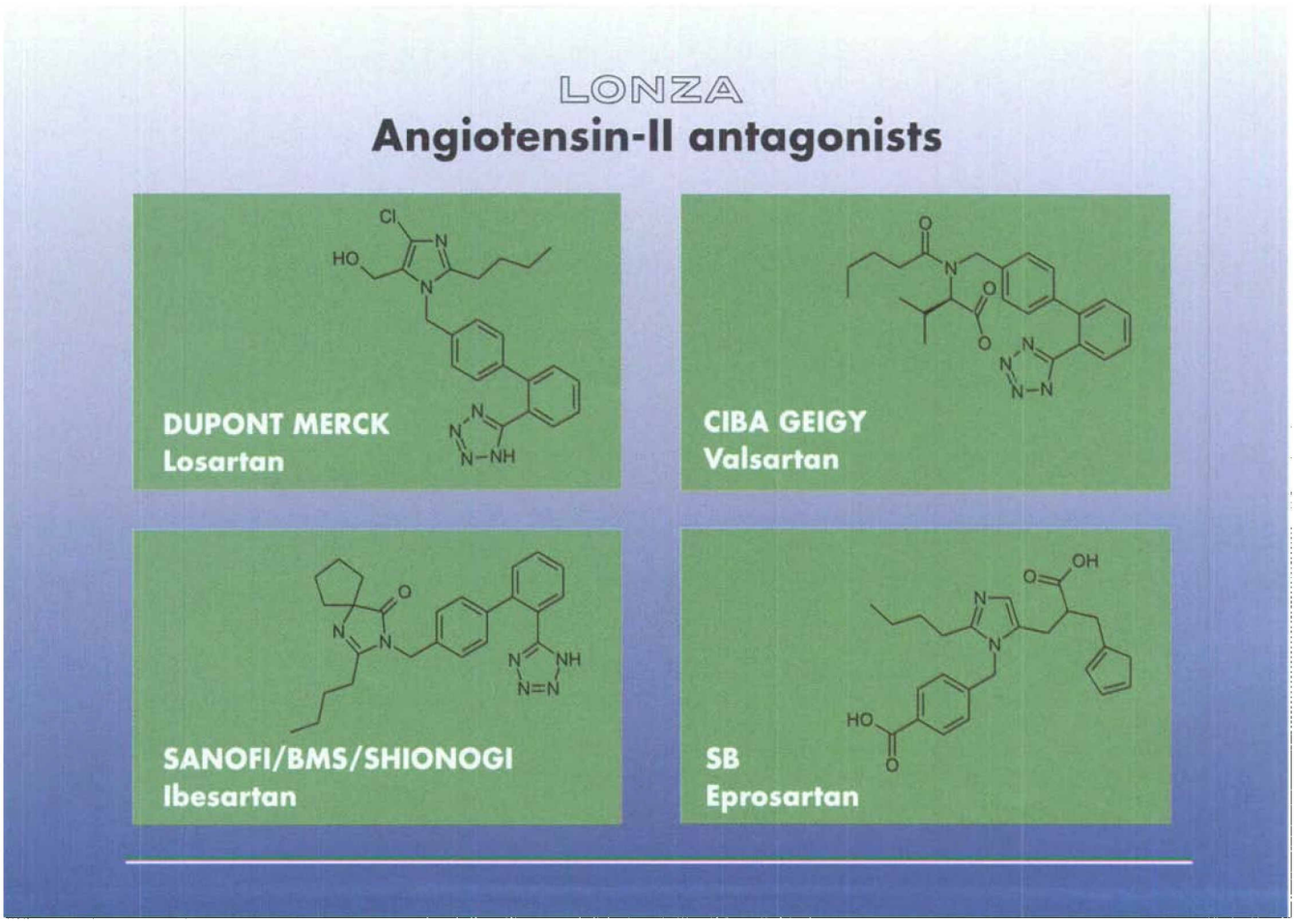


Fig. 2. *Angiotensin II antagonists*

One of the most decisive events in the last 25 years of *Lonza*'s history was related to the spectacular success of *Smith Kline Beecham*'s (at that time *SmithKline & French*) 'Tagamet'. As the in-house production capacity was totally unsufficient to cover the skyrocketing demand, a senior manager, *Ed Matthew*, travelled around the globe in order to find suppliers for different intermediates of the pharmaceutical active ingredient. *Lonza* became heavily involved in the first exclusive product for a US drug company. At the same time, purchasing departments of several progressive life science companies became weary of randomly searching for suppliers of new, commercially unavailable molecules and started to develop a technical competence within their materials management functions. Thus, *CIBA* in Basel [3] and *Merck* in Rahway developed data banks on specific technological capabilities of the leading fine chemical companies. The main reason for *Merck* partnering with us in their coccidiostat 'Arpocox' and later on in 'Primaxin' was our specific expertise in malononitrile chemistry for the former and in ketene chemistry for the β-lactam moiety of the latter. For different reasons, we are no longer involved in these chemistries, but the name tags of our first multipurpose plant in Visp and a quotation in *Merck*'s centennial book: 'The first steps took place in Switzerland' [4], keeps the memory of the beginning of our involvement in exclusive manufacture alive. Also, *Carlos Rosas*, at the time head of chemical development at *Merck*, introduced for the first time a systematic technology transfer from a customer to *Lonza*. The term 'Carlos Rosas yield' is still used in the context of exacting measures of performance in technology transfer.

The cooperation with the above-mentioned and other leading life science companies brought us to the turning point in the transition from product-driven 'supply-push' to market-driven 'demand-pull' strategy. In the connotation of outsourcing, the term 'fine chemicals' was used within *Lonza* for the first time in 1982.

This demand-pull or customer orientation affected substantially not only the R & D, manufacturing and other functions of the company, but above all top management. The management committee of our parent company, *Alusuisse-Lonza*, hitherto accustomed to approve investments for aluminium smelters, a product even present in the company's name, was confronted with a totally different situation: a capital request for a multipurpose plant, the Fine Chemicals Complex, was now presented with a 'tentative' or 'illustrative' product portfolio and rather vague figures for the further development of demand .... Without the visionary thinking of *Hans K. Jucker*, at that time president of *Lonza*, the substantial investments in the future would hardly have been approved, and we would not have become the leading exclusive fine chemical manufacturer. Yet, the dichotomy between top management expecting risk coverage from customers and customers expecting *Lonza* to share their risks inherent with launching new drugs or agrochemicals, still prevails today.

Pursuing a 'demand-pull' strategy does not mean that R & D should be restrained to apply existing technologies for the synthesis of tailor-made molecules. *Table 3* shows a number of new technologies developed by major fine chemical companies. They were successful when they

Table 3. *Fine Chemical Technologies*

Company		Technology	Products, markets	
UBE	Japan	carbonylation/alkylnitrite-catalyzed oxidation	(methanol →) carbonates, oxalates (acrolein →) 3,3-dimethoxyproprionitrile → 'Py nitrile' [a]	[c]
Sumitomo	Japan	hydroxylation *via* hydroperoxide ammonolysis	resorcinol, *m*, *p*-cresol *m*-aminophenol	
Takasago	Japan	asymmetric reactions catalyzed by 'BINAP' metal complexes	4-acetoxy-2-azetidinones, Imipenem l-Menthol	[d]
Eastman	USA	butadiene epoxidation	cyclopropanecarboxylic acid	[e]
Hoechst-Celanese	Eu	acetylation	acetaminophen, ibuprofen; drugs	
Hoechst	Eu	*Heck* reaction: vinyl substitutions with organo-Pd intermediates	naproxen, sulindax; drugs CGA-152005, herbicide; ZD-0870, antifungal	
		denitrating chlorination	fluoroquinolones (lomefloxacin, cyprofloxazin), antibiotics	
Shell	Eu	Feast[b]) olefin disproportionation process	1,5 hexadiene, ...	[f]

[a]) 5-amino-2-methylpyrimidine-5-carbonitrile, precursor of Vitamin B_1.
[b]) Further exploitation of advanced *SHELL* technology.
[c]) The technology was not successful for the manufacture of malonates based on ketene.
[d]) Modifications of this technology were developed by other companies, *e.g.* by *LONZA* for the synthesis of biotin and *Novartis* for Prosulfuron, see *Chimia*, **1996**, *50*, 103.
[e]) Also considered for THF, γ-butyrolactone, and butane-1,4-diol, see *David Denton et al.*, *Chimica Oggi/chemistry today*, May 1996, p. 17, 18.
[f]) *SHELL Fine Chemicals* built a plant in Berre, Southern France, but had to shut it down because of lack of demand for the products.

Table 4. Biotransformation Processes for Fine Chemical Synthesis [5]

Company		Technology	Products, markets
Nitto	Japan	immobilized hydratase	acrylamide, paper sizing agent
Tanabe	Japan	immobilized aspartase	aspartic acid (→ aspartame)
Kaneka	Japan	immobilized decarbamylase	D-(*p*-hydroxyphenyl)glycine (→ amoxycilline)
DSM/Tosoh	Eu/J	thermolysin protease process	aspartame, sweetener
LONZA	Eu	γ-butyrobetain hydroxylase	L-carnitine, food & feed additive
Chiroscience	Eu	bioresolution	naproxen, antiarthritis drug
Zeneca	Eu	ethyl-chloroproprionate esterase	(*S*)-α-chloropropionic acid (→ arylpropionate) herbicides

provided a more economoic access to molecules for which a real demand existed.

Also in a number of distinct cases, biotransformation successfully substituted for classical organic synthesis (*Table 4*). At *Lonza*, apart from running a large-scale L-Carnitine plant at Kourim, Czech Republic, we included biotransformation in our technology arsenal for exclusive synthesis and are actively working on chiral moieties for a number of promising antiviral compounds.

In order to make the life science industry aware of our capabilities and to align the development of our core technologies with market demand, we tried to open a dialogue with the chemical development departments of our customers. Although purchasing was sometimes reluctant to establish these contacts, the potential mutual benefit was recognized in most cases. With the valuable support from our researchers, *Lonza* presentations to mixed audiences were tailored to expected customer's needs. In most cases, there was no immediate response. Nevertheless, they allowed the establishing of personal contacts, and sometimes valuable inquiries came in much later.

... to a Partner of the Global Life Science Industry for Sophisticated Fine Chemicals.

With this approach we had gone about halfway between a nonexisting supplier/customer relationship at the beginning (carbide and fertilizers were ordered from a price list) and a true partnership involving joint teams representing R & D, manufacturing, commercial, legal and financial experts from both companies. A strategy for our exclusive business was formulated in 1988. In order to communicate our new and focussed approach to the life industry, the slogan 'Leave it to *Lonza*' was coined. A key element was a staged approach to joint projects (*Fig. 3*).

Thus, after signing a secrecy agreement and carefully reviewing the 'technical package' provided from the customer partner by in-house experts, a detailed offer named 'project proposal' was prepared (*Fig. 4*). The objective was obviously to convince our counterpart on the basis of solid facts or at least viable assumptions, that *Lonza* was the right choice ..., and it did work in many instances. After acceptance by the customer, R & D work was initiated and joint project teams were formed. These teams were the beacon of a new era in the relationship with our customers, *i.e.* partnership.

In the former one-way information approach, we proactively proposed new molecules based on a desk research to our customers. This was often to their and our exasperation, because in most cases, they had no idea about, not to mention requirement for the funny molecules we proposed. Out of this situation, a partnership with the customer evolved through a two-way information flow (*Fig. 5*).

Partnerships of this kind are best defined as: 'A close long-term relationship, where customer and supplier work together to secure for each other and the end customer the best sustainable commercial advantage' [6]. They constitute the way to go for complex fine chemicals, where there is a one-product/one-customer situation, where proprietary technology and intellectual property rights are involved, where specifications and impurity profiles are mutually agreed upon, where regulatory support is required in order to accelerate time-to-market, and where – last but not least – there is no market price but a jointly agreed upon cost plus price with a formula for sharing process improvements. Whereas in traditional customer/supplier relationships prices are negotiated on pure commercial terms between purchasing and sales ('market price less' principle), the determination of the price is now based on a 'cost plus' mechanism, elaborating on the cost structure of the product. This can go as far as an 'X-raying' the whole supply chain by controllers. Items such as overheads allocation (R & D, process improvement, analytical services, maintenance, waste treatment ...), shared services, raw-material costs, and transfer prices for products from other divisions/plants are looked upon.

This approach does not apply to the great majority of business transactions in the chemical industry, where readily available commodities from many suppliers are involved, but only to a tiny fraction of it, not exceeding a few percentage points of the total turnover of the chemical industry which is estimated at USD 1500 billion.

Although there are impressive benefits of partnerships (*Table 5*), they are also potential dangers and pitfalls, such as proliferation of confidential know-how, large resource requirements for joint teams (*cf.* the above-mentioned mechanisms for the price determination) and overdependency.

The item 'most cost-effective supply' mentioned in *Table 5* obviously surfaces frequently in discussions with our partners. It is therefore worthwhile to explore this in somewhat more detail. The two most important facets are:

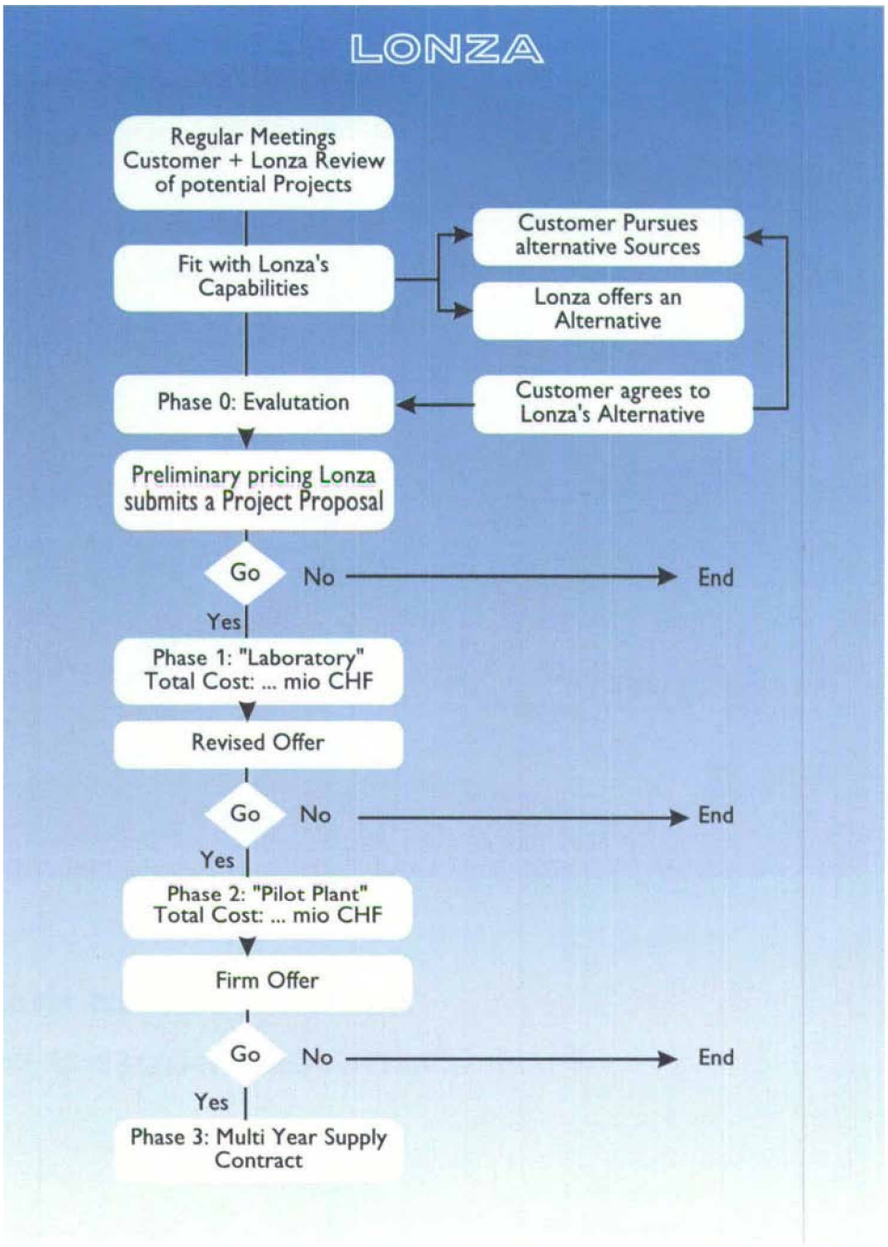


Fig. 3. *Schedule for joint projects*

Table 5. *Benefits from a Strategic Alliance*

Life Science Company	*LONZA*
• additional creativity	• more business opportunities
• freeing of in-house resources	• access to more products in customer's R & D pipeline, including right of first refusal
• faster development	• supplying throughout the life cycle due to maintained competitiveness
• more cost-effective development	• better risk assessment through sharing of information
• more cost-effective supply	• better utilization of resources
• more flexible capacity	
• elimination of non-value-added activities	
• continuous improvement in cost	

Joint **Life Science Company & LONZA**

• both companies improve their business performance
• Win Win

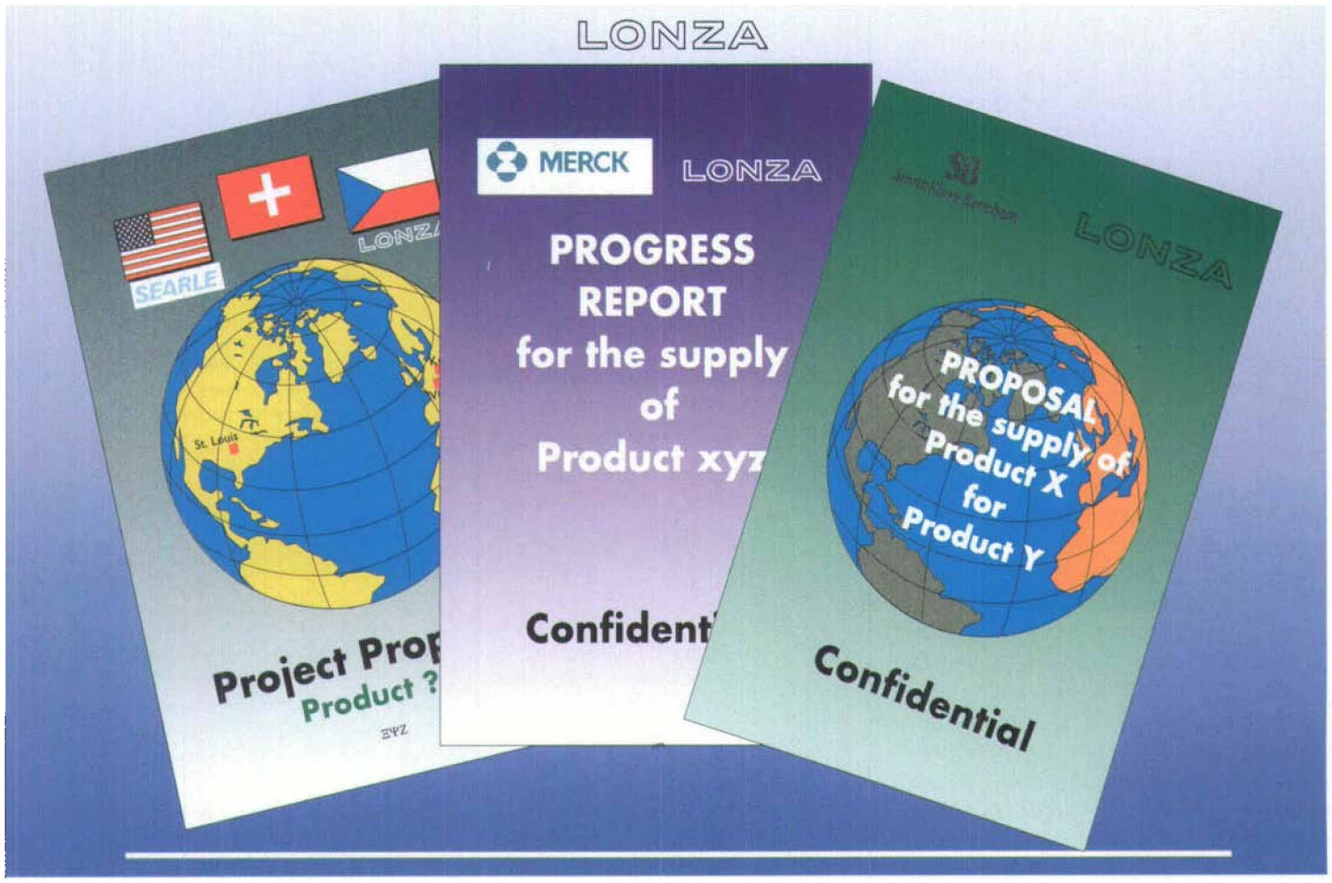


Fig. 4. *Project proposals*

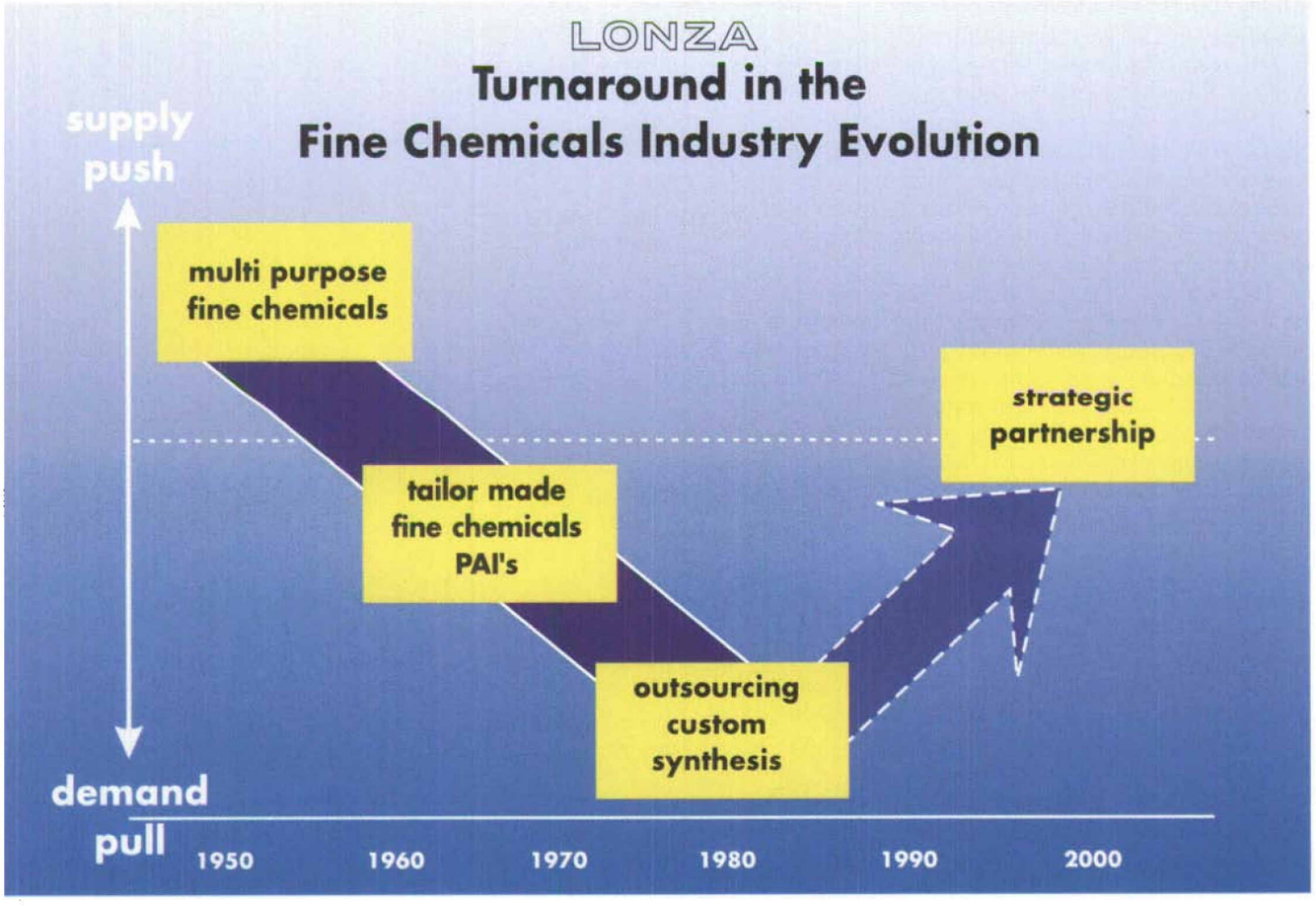


Fig. 5. *Evolution of the* LONZA-*customer interface*

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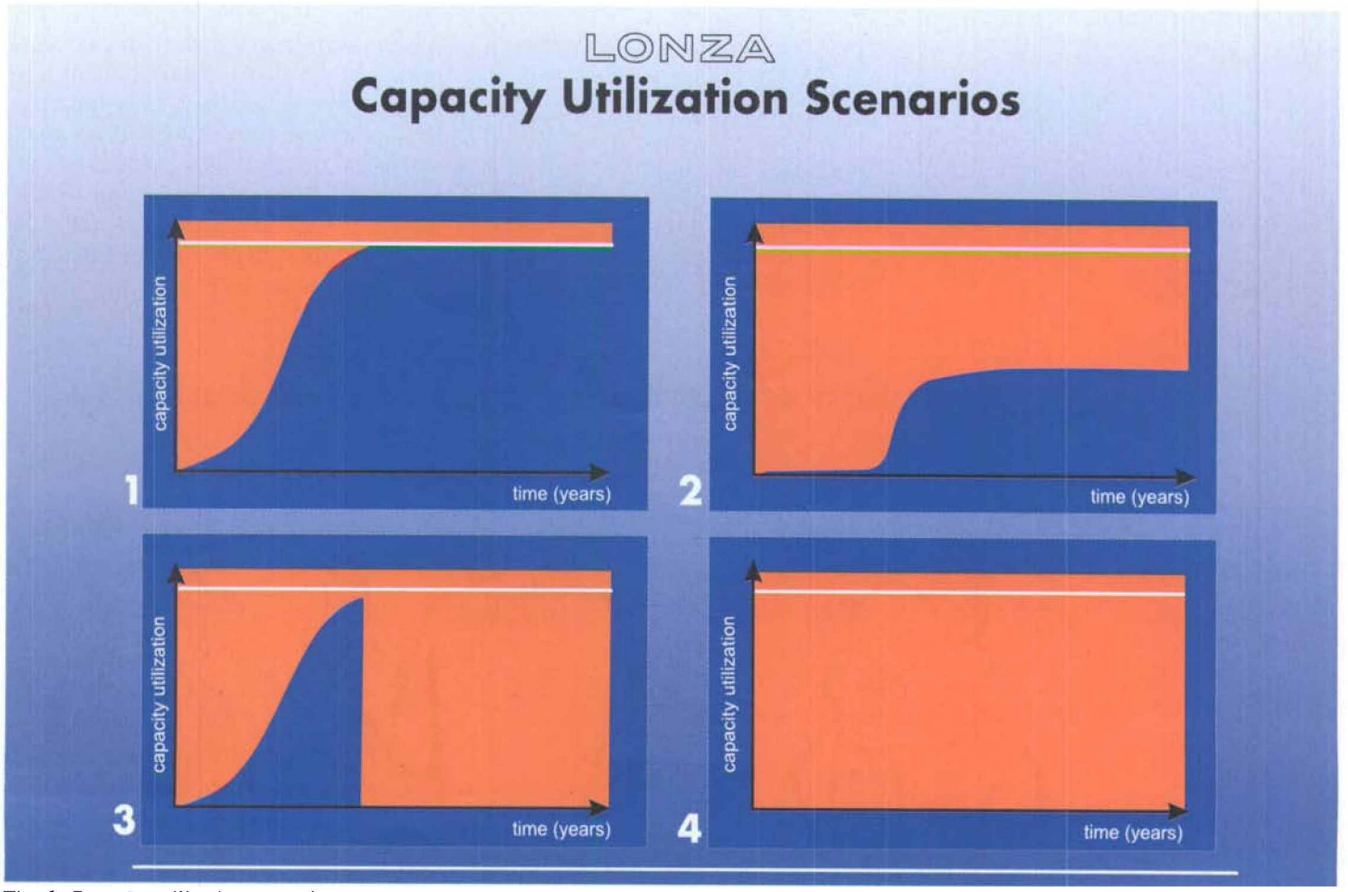

Fig. 6. *Capacity utilization scenarios*

scenario		idle capacity
1	according to plan: FDA approval in time, anticipated demand is reached rapidly	only during ramp-up
2	launch delayed and anticipated capacity not reached, *e.g.* because of advent of competitive products	substantial
3	product and process, resp., is abandoned, *e.g.* because of development of side effects and new technology, resp.	substantial
4	product does not make it to the market place, *e.g.* because FDA does not approve	total

- *Capacity utilization*: Life science companies usually have difficulties in achieving a good capacity utilization and therefore a good return on their capital-intensive plants. The prime reason for this is that even the largest ones rarely have more than one new chemical entity (NCE) approved by the FDA in one given year [7]. We are in a more favorable position, as we can lever positive and negative deviations from plans for single projects (see scenarios 2, 3, and 4 in *Fig. 6)*, because we have access to the new product pipeline of several companies, smoothing the volatility of volume requirement for one single product. This leads over all to a better capacity utilization [8] and lower costs of goods.
- *Economy of scale*: Here again, we can pool requirements for specific core technologies [9] required for products from different customers. By this way, larger, more cost-effective facilities can be built and operated.

Next to financial considerations, the safeguard of mutual intellectual property rights is another key requisite for a successful partnership. Here too, a dramatic evolution has taken place during the 100 years of existence of *Lonza*. Up to the late 50s, not only the R & D activities, but also the product portfolio [10] was kept totally secret and stonewalled not only against competitors and customers, but even against other groups within our company! Now the 'wall of silence' has been widened to include the customer partner (*Fig. 7*). Under the umbrella of a confidentiality agreement, information on products, processes, applications, *etc.* is shared in order to better focus the joint tasks. Assisting our partners in maintaining their competitive advantage by protecting the know-how against their competitors is gaining importance.

Now, endeavoring to cope with fundamental changes occuring in an increasingly competitive environment [11], another paradigm shift becomes apparent: the emergence of 'The Virtual Pharmaceutical Company' (*Table 6*). It outsources even what hitherto have been considered core competences, such as discovery, development, and marketing of new drugs ...

- the NCE (licensing-in, *e.g.* from a university),
- clinical testing,
- developing of the manufacturing process,
- development of the galenic form and formulation,
- registration,
- industrial scale primary and secondary production,
- marketing and sales.

Even the leading life science companies will be affected by this trend: Downsizing to remain competitive, accelerating time-to-market to benefit from patent life and other initiatives foster a more rigorous concentration on core competences. Thus, in primary pharmaceutical or agrochemical manufacturing, outsourcing will no longer be limited to custom or toll manu-

Table 6. *US Virtual Pharmaceutical Companies*

Aronex Pharmaceuticals, Inc.	The Woddlands, Texas
Hillman Medical Ventures	Horsham, Pennsylvania
Orphan Medical	Minnetonka, Minnesota
RGene Therapeutics	Seattle, Washington
Sun Pharmaceuticals	Jacksonville, Florida

facturing, *i.e.*, receiving a fully developed process, adapting it to the particular constraints of a plant, ramping it up, and running it on industrial scale. In the future, fine chemical companies will be asked more and more to supply sample quantities and develop suitable chemical processes as well. In other words, asking the supplier partner to participate earlier on in the chemical development effort and to

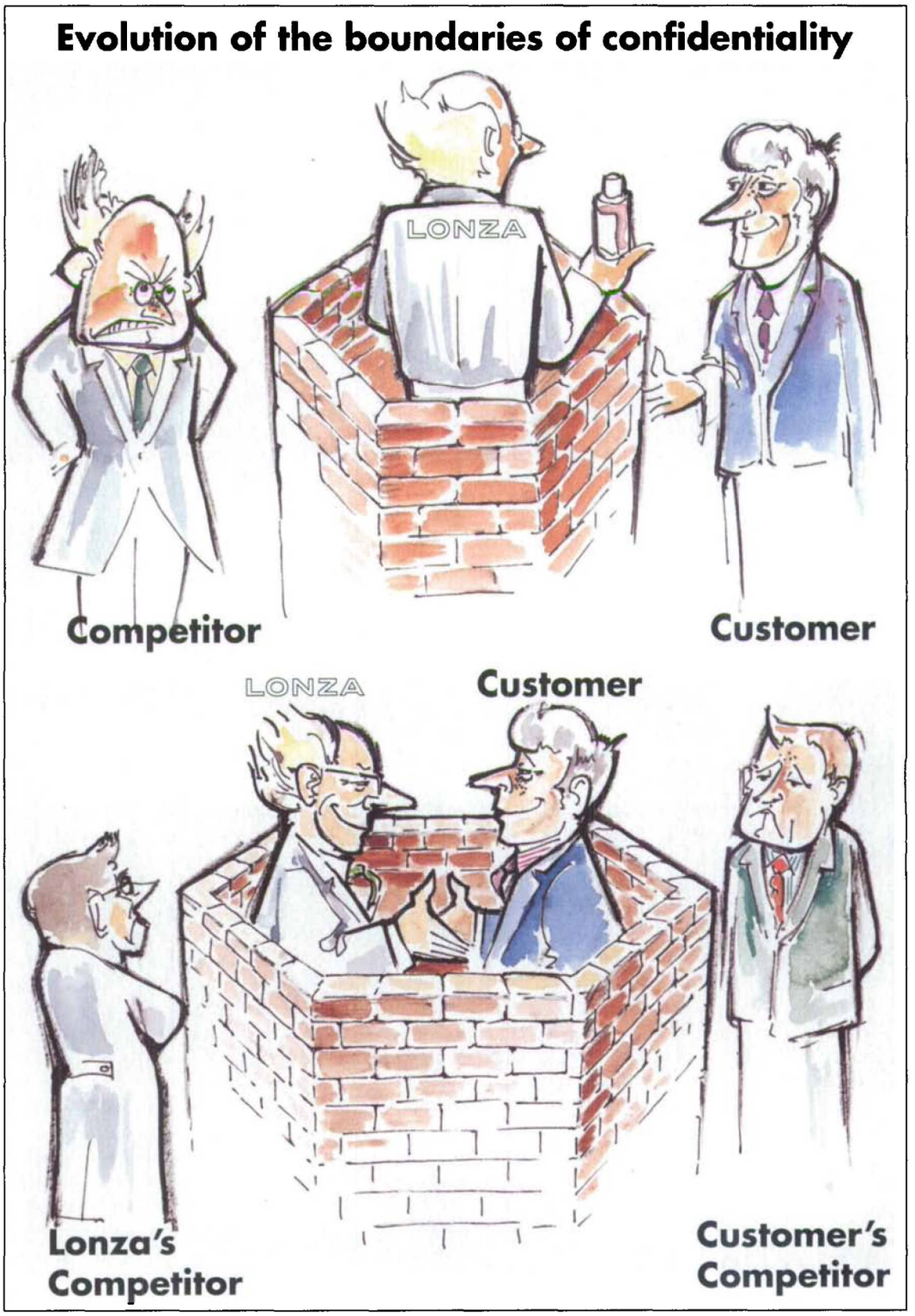

Fig. 7. *Evolution of the boundaries of confidentiality*

share the pain and the glory of NCE development ...

The consequences cannot yet be fully assessed. The main differences with the traditional scheme for exclusive projects are the high drop-out rate of early-stage projects (Pre IND, Phase I, ...) and the long-time lapse between start of R & D for a new product on the one hand and start of industrial scale production (if at all) on the other hand. Whereas up to now R & D costs for new projects were recovered once the product went into industrial scale production, this is no longer viable with the 'early on' scheme. Under typical assumptions, the net present value of such a project will be negative if it is initiated prior to phase II (*cf. Fig. 8*) [12].

Therefore, a new model will have to be developed for charging R & D expenses up-front. R & D, traditionally considered primarily as a support function in the fine chemical industry, will play a different role by becoming a profit center of its own.

This 'earlier on' involvement is only one aspect of *Lonza*'s broadening the offer approach. It also includes:

- Geographical extension. It began with the acquisition of *BAIRD Chemical* in 1968, went on by opening sales offices in key industrialized countries from the 80s onwards, and will continue at a more rapid pace by establishing production platforms in the Far East [13] and expanding our US fine chemicals plants. Production from the latter should cover 50% of our sales in the United States by 2005.
- Adding technological competences. Apart from innovative research in traditional organic synthesis, three big steps have been taken here by establishing a stake in biotechnology: Taking up biotechnological research in the 80s, acquiring *Kourim* in 1992, and most recently *Celltec* (now *Lonza*) *Biologics*.

Lonza, dealing proactively with these most recent developments, demonstrates its continued ability to anticipate changes in the business environment. Thus, we are well prepared to continue our role in the center of gravity of the chemical industry (*Fig. 9*).

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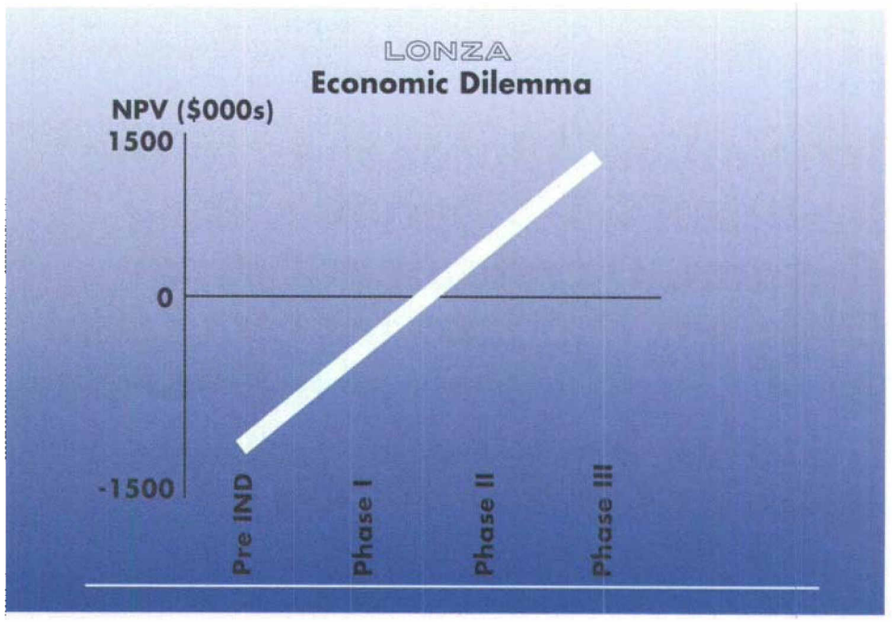

Fig. 8. *Economic dilemma of 'early on' projects*
assumptions:
- USD 1 Mio. investment in R & D
- standard pharmaceutical pipeline success rates
- 3 years drug development
- 10 years sales of commercial quantities
- sole supplier status

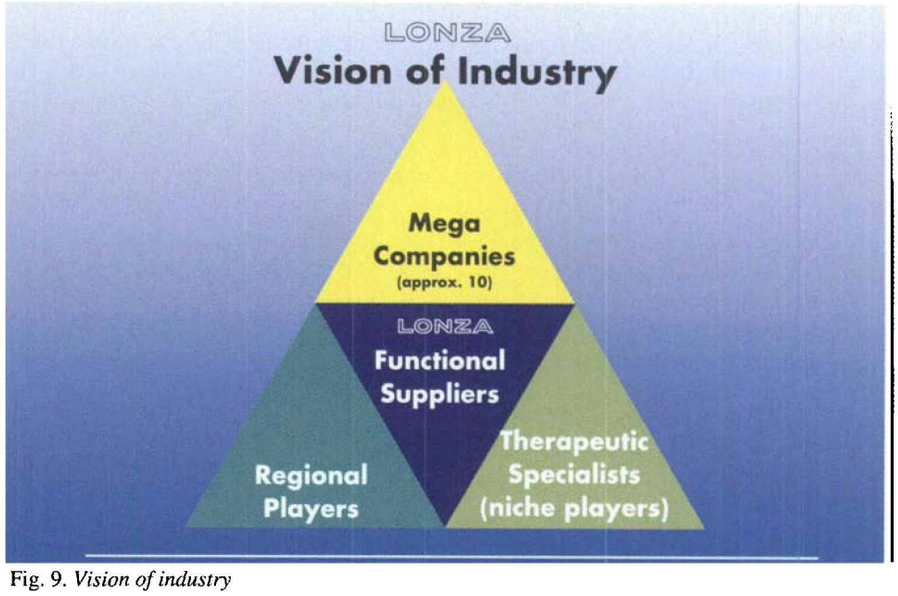

Fig. 9. *Vision of industry*

[1] See also G.C. Stucky, *Chimia* **1997**, *51*, 280.
[2] The engineers from the licensor, *SHELL*, jokingly called our plant a 'pilot plant'.
[3] A. Restelli was rumored to have developed a complete product flow chart ouf our Visp plant.
[4] 'Values & Visions, A *Merck* Century', 1991, p. 126.
[5] H.-P. Meyer, *LONZA*.
[6] *Zeneca*, Fine Chemicals Conference, London, Nov. 20, 1996.
[7] There are 40 pharmaceutical companies with sales more than USD 1 billion, whereas the FDA typically approves *ca.* 30 NCEs per year, leading to a statistical average of less than 1 NCE/company/year.
[8] For a detailed discussion of this subject see: Peter Pollak, 'Fine Chemical Manufacturing' in 'Kirk-Othmer, Encyclopedia of Chemical Technologie', 4th edn., Vol. 10, p. 900–917, J. Wiley & Sons, Inc., 1994.
[9] *E.g.* cyanogen chloride, ketene, metal organic reactions, catalytic hydrogenation, particular waste disposal processes.
[10] Instead of the commercial product designations, secret names were used such as 'azol' for acetic acid, 'anol' for acetic anhydride, 'dianol' for diketene, 'monazol' for methyl acetoacetate, and 'diazol' for ethyl acetoacetate.
[11] Environment both in terms of environmental regulations and business conditions.
[12] S. Lehrer, 'Managing Technology in an Evolving Fine Chemicals Market', Fine Chemicals Conference, London, Nov. 20, 1996.
[13] Niacinamide (nicotinic-acid amide) in China and isophthalic acid in Singapore.