

Leonardo da Vinci Transfer of Innovation Project

„Transfer of experiential and innovative teaching methods for business education“

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Fermentas: from Research Idea to the Market

Case study

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Molecular biology products for researchers, created and manufactured by „Fermentas“, may not attract the media attention, but the results they help to produce, do.

The German newspaper Süddeutsche Zeitung reported that scientists had discovered that the O104:H4 bacteria responsible for the current outbreak is a so-called chimera that contains genetic material from various E. coli bacteria. It also contains DNA sequences from plague bacteria, which makes it particularly pathogenic. The bacterium that is currently terrifying the country is an enterohemorrhagic strain of the bacterium Escherichia coli (EHEC), a close relative of harmless intestinal bacteria, but one that produces the dangerous Shiga toxin.

Helge Karch, the director of the Robert Koch Institut's EHEC consulting laboratory at the Münster University Hospital in western Germany, has devoted almost his entire life as a researcher to EHEC bacteria. "But I've never encountered something like this," he said.

(Spiegel Online International, May 31, 2011

<http://www.spiegel.de/international/germany/0,1518,765777,00.html>)

In October 2005 Ramutė Pinelienė, a researcher at „Fermentas“ research center, finished preparing project documents for a meeting of the New Product Committee. After spending several months on plasmid DNA purification trials, Ramutė was confident that her idea – Plasmid Miniprep Kit – would significantly facilitate the work of researchers and therefore would be a product able to find its buyers. However, Ramutė knew that only about 5% of ideas in “Fermentas” translated into commercial products. Will her Plasmid Miniprep Kit become one of them?

Company background

Starting in 1975 in Vilnius as a small laboratory of young Lithuanian scientist Arvydas Janulaitis in soviet-time research institute, “Fermentas” has developed to a world-known biotechnology company discovering, producing and selling molecular biology products for life science research and diagnostics. Fermentas brand is known for its leading line of restriction enzymes and DNA ladders and molecular weight markers. Since its 30-year history “Fermentas” scientists have discovered approximately one third of all known restriction enzymes. Fermentas competes with the leading biotechnology companies, such as Life Technologies, Bio-Rad, New England Biolabs, Promega, Roche, Applied Sciences, Takara. During the period from 1995 to 2005, UAB „Fermentas“ sales grew rapidly from 7m Lt to 37,5m Lt (from €2m to €10,9m). Revenues of „Fermentas International“, a holding company of UAB „Fermentas“ and its joint companies in USA, Canada and Germany, reached €17,7m in year 2005. All the time Fermentas business was profitable and enabled significant investment in fundamental and experimental research. An investment of €2,2m (= \$2,63m.) in 2005 represented 80% of Fermentas net income.

The company employs 500 professionals worldwide and has its own network of 50 distributors, covering 70 countries. Company' strategy is oriented towards innovations:

creation of new products and technological improvements. All products have to pass a "Pure-Extreme" quality test that was created by Fermentas in 1996 and set a new and stricter standard of product quality than its competitors.

Fermentas' New Product Committee

The company's portfolio has grown to 760 products, most of which were developed in its own laboratories. Approximately half of 150 employees work in research and development. At any single time „Fermentas“ has about 5-12 new product development projects. So, the New Product Committee (NPC) at „Fermentas“ is never out of work. For a better control of the new product development process, a "Stage-Gate" management system was implemented in the company in 2004. This has reduced the number of ideas being developed into products from 20 out of 100 to only about 3-4 out of 100. „Stage-Gate“ system became an integral part of „Fermentas“ organizational culture. Every idea, suggested by research center scientists, is carefully evaluated to decide whether it can be turned into a commercial product. NPC is a team of „Fermentas“ experts from various functional fields. Its role is not only to evaluate the scientific idea, but, most importantly, the product's potential in a competitive market. The committee decides whether the company should continue the new product development project. If the potential is evaluated positively, then NPC experts recommend which product features should be researched and developed further, and plan next steps in product manufacturing trials and marketing.

Meeting on the Plasmid MiniPrep Kit project (October 2005)

On her way to the New Product Committee meeting, Ramutė hoped that the experts would meet the Plasmid Miniprep Kit idea positively. She was ready to continue research until her idea would be turned into a product ready to be released to the market. Ramutė also expected to hear many critical questions and advice from her colleagues. The NPC comprised company' managers and founders, scientists prof. Viktoras Butkus and prof. Arvydas Janulaitis, business development director Algimantas Markauskas, marketing representative Edita Šmergelienė, project manager Jūra Žilytė and a number of Ramutė's fellow researchers. All of them had plenty of experience in inventing and developing new reagents, as well as in their manufacturing and commercialization.

As expected, the New Product Committee first asked Ramutė to present briefly the idea of the product. Ramutė started her well-prepared pitch:

“Scientific laboratories which research DNA from various bacteria need a product which would allow convenient isolation of high quality DNA fast and efficiently. My idea is the Plasmid Miniprep Kit, which could be used for the isolation of DNA from *E.coli* cultures. Using the kit, the procedure is fast – less than 15 minutes. It is also efficient – up to 20 µg of high quality plasmid DNA can be recovered from 1-5 ml of bacterial culture.“

„How does that Plasmid Miniprep Kit work?“, asked Jūra Žilytė.

„The kit will contain a number of different solutions, spin columns, and tubes. First, the researcher harvests a *E.coli* bacterial culture. Then *Lysis solution* is used to break cells by melting membranes. *Neutralization solution* is applied and the centrifugation is done in the

spin column. DNA accumulates on the walls. *Wash solution* washes away the contaminants, while pure DNA is melted using *Elution Buffer*. The purified plasmid DNA is ready to be researched“, explained Ramutė.

Edita Šmergelienė from marketing had done the preliminary market analysis and presented it to the committee: „No doubt spin column-based Plasmid Miniprep Kits will fit perfectly with Fermentas product line. Having kits of our own will make troubleshooting of our existing products easier. From a marketing point of view, I would suggest developing the proposed kits and adding them to Fermentas product line.

„The main player in the DNA purification kit’s market is Qiagen, they control about 2/3 of the market. A preliminary estimate of the global market size for Miniprep kits is about \$133 million dollars. Fermentas usually aims for a 1% market share. However, what are the competitive advantages of your proposed kit, Ramutė? What are the main features of competitors’ products and how will our product differ from them?“ Like how you weave characters into the case and use quotes from them to highlight areas for discussion and debate

Ramutė mentioned that the main competitors would be Qiagen and Sigma, but had to admit that market research was still at an early stage, and further competitors’ product analysis needed to be done.

Business development director Algimantas Markauskas continued the discussion: „This product matches the strategic goals of our company, since it is oriented towards extending product supply in the area of DNA purification. In my opinion, this Miniprep kit has potential“.

Prof. Arvydas Janulaitis asked: „Your proposed kit will contain spin columns. We do not currently produce them. Ramutė, how do you suggest we obtain them?“

„Well, I thought the spin columns could be bought from a supplier in China“, said Ramutė.

„We need to ensure high quality of our products. If we buy the columns from China, how can we guarantee their quality?“, doubted Arvydas Janulaitis.

„I am also concerned about that“, admitted Ramutė. „After visiting suppliers in China, we familiarised them with spin column manufacturing technology. The supplier has quality certificates. However, that does not guarantee that the quality of spin columns from individual lots will not differ.“

Algimantas Markauskas pointed out: „Well, if product sales grow satisfactorily, maybe we can consider the possibility to manufacture such columns ourselves ?“.

„That is an option“, agreed Viktoras Butkus.

Questions and discussions continued for a while. Finally, NPC experts agreed that Ramutė’s idea had potential, and decided to go forward with the project. Nearly everybody had some tasks for new product development. It was agreed to complete them by January 15, 2006.

Ramutė continued researching the features of the product and comparing them with competitors' kits. Edita Šmergelienė took the responsibility for market research and investigation of competing products' prices. Gražina Mikšytė, together with Ramutė and Edita, had to collect data for marketing materials, to compile the manual of the Miniprep Kit, and to prepare information for the website and for the product catalogue.

After the meeting Ramutė was tired but happy. Her idea had convinced the committee. It seemed that there was a chance to get into that selective group of 5% ideas that make it as commercial products in „Fermentas“. She resolved to work hard to achieve this, and went back to her lab with enthusiasm.

2nd meeting of the New Product Committee (January 17, 2006)

A project team consisting of Ramutė, Edita and Gražina attended the second NPC meeting, ready to answer all the questions that had been raised in the October meeting.

This time the NPC experts spent a lot of time discussing various technical characteristics of the Plasmid Miniprep Kit. Ramutė had performed lots of tests in her lab and was well-prepared to explain all the details.

L. Grinius joined the discussion: „For nearly a decade we market our products as satisfying the „PureExtreme“ quality standard. Have you researched how many albumen there are in purified plasmid DNA?“

„Yes, of course“, ensured Ramutė. „The level of albumen was tested with A260/A280 ratio, and the result was 1,77-1,9. Such value shows that the resulting DNA does not have albumen contamination. I got similar results using kits of our competitors, namely Qiagen and Promega.“

„I think you should continue testing using different methods. We have to be sure the „PureExtreme“ quality standard is met“, L.Grinius seemed not convinced.

Business development director Algimantas Markauskas said: „Well, since the DNA purification procedure is fast, that is already a strong argument in favour of „PureExtreme“.“

After the technical details were discussed, Edita Šmergelienė presented competitors' price analysis and other marketing research results. The committee was satisfied with the project team's work. After lengthy discussions experts decided that the Plasmid Miniprep Kit should be marketed focusing on the following product features:

- **High quality** of purified plasmid DNA which enables fast analysis in all conventional molecular biology procedures;
- **Fast** purification procedure;
- **Efficiency** (yields up to 20 µg of plasmid DNA).

Towards the end of the meeting, the finance director of Fermentas raised an important question: “Do you think such product could be profitable?”

Ramuté had evaluated preliminary costs for a kit necessary for one preparation, so she was ready to answer: “Yes, I do. The manufacturing costs are approximately \$0,20 per preparation. This would allow both a competitive price and a sufficient margin”.

However, the finance director was not entirely convinced. He left the meeting with an unanswered question, which needed to be investigated further:

Can we expect that the new product will be profitable enough for the company?

Appendix 1

Plasmid Miniprep Kit (extract from the brochure at www.fermentas.com)



Applications

Fast and easy isolation of high quality plasmid DNA suitable for all conventional molecular biology procedures, including:

- FastDigest® DNA cleavage
- Conventional restriction digestion
- PCR, fast PCR
- Automated fluorescent sequencing
- Conventional radioactive sequencing
- Transformation
- *In vitro* transcription (see www.fermentas.com for recommendations)

Kit Components

- GeneJET™ Spin Columns assembled with Collection Tubes
- Resuspension Solution
- Lysis Solution
- Neutralization Solution
- Wash Solution (concentrated)
- RNase A Solution
- Elution Buffer

Appendix 2

Price analysis of Plasmid Miniprep kits (prepared by Edita Šmergelienė)

Priedas 4.2 prie projekto GM/2005/ Plazmidžių gryninimo rinkinys

Price analysis: Plasmid miniprep kits

Company	Product	Cat#	principal	time	Size (preps)	Price USD	USD/ prep	Price Eur	Eur/ prep
Qiagen	QIAprep Spin Miniprep Kit	27104	silica membrane	24 preps in 30min, 20µg	50	67	1.34	73	1.46
		27107			250	290	1.16	324	1.30
Promega	Wizard® Plus Minipreps DNA Purification System	A7100	resin	15min, 10µg	50	90	1.80	70	1.40
		A7500			100	131	1.31	143	1.43
		A7510			250	310	1.24	299	1.20
	Wizard® Plus SV Minipreps DNA Purification System	A1330	silica membrane	20µg, 20 preps in 45 min	50	56	1.12	62	1.24
		A1460			250	246	0.98	265	1.06
Invitrogen	ChargeSwitch® NoSpin Plasmid Micro Kit	CS10201	magnet	15min, 5µg	96	219	2.28	119	1.24
		CS10201-10			960	1728	1.80	952	0.99
	PureLink quick plasmid miniprep kit	K2100-10	silica membrane	45 min, 40µg	50	55	1.10	73	1.46
		K2100-11			250	240	0.96	324	1.30
	SNAP miniprep kit	K1900-01	resin	25min, 10µg	100	259	2.59	261	2.61
Sigma	GenElute Plasmid Miniprep kit	PLN10	silica membrane	24 preps in 30min, 20µg	10	17.7	1.77	18.4	1.84
		PLN70			70	68.6	0.98	68.7	0.98
		PLN350			350	295.4	0.84	309.6	0.88
	GenElute Five-Minute Plasmid Miniprep Kit	PFM10	column	5min, 5µg	10	NA		NA	
		PFM50			50	NA		NA	
		PFM250			250	NA		NA	
Bio-Rad	Aurum mini kit	732-6400	silica membrane	10min, 20µg	100	135.00	1.35	267.0	2.67
	QuantumPrep MiniPrep kit	732-6100	diatomaceous earth	15min, 20µg	100	125.00	1.25	160	1.60
Eppendorf	Perfectprep® Plasmid 96 Spin Direct Bind Kit	955150406	plate	192 samples in 65min	192				
		955150414		384 samples in 75 min	384				
	FastPlasmid™ Mini Kit	955150601	column	20µg in 9min	100				
		955150619			200				
GE Healthcare	GFX Micro Plasmid purification kit	27-9601-02	column	18 preps in 30min, 2-6µg	250	264	1.06	263	1.05
Macherey-Nagel	NucleoSpin® Plasmid	740588.10	silica membrane	25µg, 18preps in 25 min	10				
		740588.50			50				
		740588.250			250				
	NucleoSpin Plasmid QuickPure	740615.10	silica membrane	15µg, 18 preps in 11 min	10	15	1.50		
		740615.50			50	54	1.08		
		740615.250			250	230	0.92		
Stratagene	StrataPrep plasmid Miniprep Kit	400761	silica membrane		50				
		400763			250				
Median Market price					10		1.60		
					50		1.05		
					250		1.00		

Appendix 3

Fermentas Financials

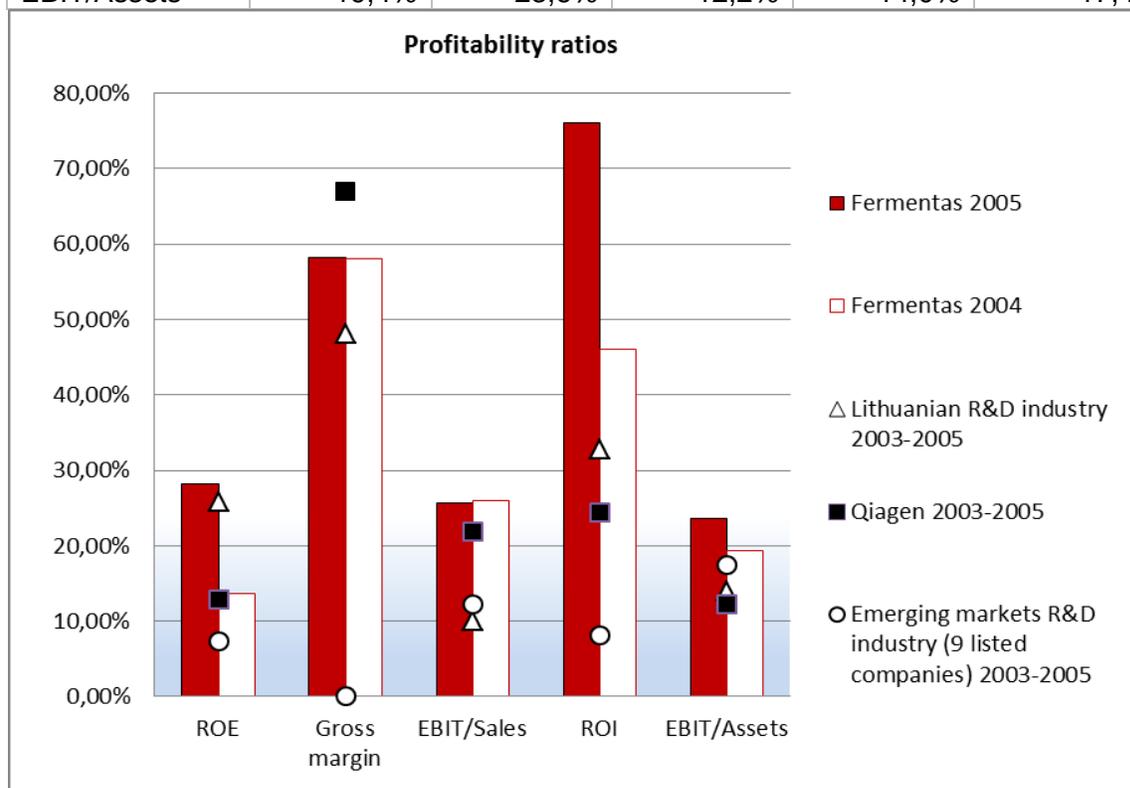
Balance sheet	Y. 2005, m\$	Y.2004 m\$
Total Assets	14.03	16.67
Intangible Assets (excluding goodwill)	0.59	0.33
Equity	11.68	15.13
Long Term Lease Liabilities	0.07	0.11
Current Lease Liabilities	0.11	0.07
Income Statement	Y. e. 2005	Y.e.2004
Revenues	12.87	10.81
Gross Profit	7.49	6.27
EBIT	3.30	2.81
Income Taxes*	0.62	0.44
Net Income	3.29	1.79
Cash Flow Statement	Y. 2005	Y.2004
Depreciation and Amortisation	0.91	0.84
Investments in Long Term Assets	-1.50	0.68
Dividend Payments	4.78	0.00
Repayments of Finance Lease Liabilities	0.08	0.03
Interest Payments	0.01	0.03

*Average tax rate was 17,2%

Appendix 4

Financial ratios for comparison

Financial Ratios	Fermentas 2004	Fermentas 2005	Qiagen 2003-2005	Lithuanian R&D industry 2003-2005	R&D industry of emerging markets (9 listed companies) 2003-2005
ROE	13,6%	28,2%	12,9%	25,9%	7,3%
D/E	0,01	0,02	0,71	1,22	0,37
Gross margin	58,0%	58,2%	67,0%	48,1%	ND
EBIT/Sales	26,0%	25,7%	21,8%	10,0%	12,2%
ROI	46,1%	76,1%	24,4%	32,8%	8,2%
EBIT/Assets	19,4%	23,6%	12,2%	14,0%	17,4%



Cost of capital data for the global Biotechnology market, 2005

	Long- term treasury bond rate*	Beta	Risk Premium for Equity	Book D/E	Cost of Equity	Cost of Debt	Cost of Capital
87 listed companies	4,39%	1,63	4,80%	0,57	12,23 %	7,84%	8,47%

*Country risk premium for Lithuania 1,35%