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*Dr Kurt Wüthrich received the 2002 Nobel prize in Chemistry for his work on biomolecular structures in solution using NMR, and this cover is inspired by his work.

http://www.nobel.se/chemistry/ educational/poster/2002/index. html



The connecting thread

Regardless of how one looks at the exacting discipline of drug discovery.

As a simple or a cryptic process.

A result of chance, of serendipity, thoughtful luck. Or perhaps the outcome of a disciplined, carefully detailed, systematic approach.

Regardless of the approach, for an advance to gather meaning and context it has to bind to, and impact real life. It has to move out of the clean room environment of a lab and make a real time difference.

Perhaps rescuing a Van Gogh from the murky quicksand of schizophrenia.

Perhaps recognizing the wisdom, despair and beautiful mind of yet another John Nash.

Supporting, nourishing life. Making a return to baseline possible.

The cover design uses two elements- the fingerprint of a molecule as decoded by an NMR*, and the human brain.

With NMR, the structure of a substance can be worked out by studying the spectrum that results in a strong magnetic field, when pulses of radio waves are beamed into a sample. Since each atomic nucleus causes one or more peaks, a large structure gives rise to a very complicated spectrum with numerous peaks. By measuring these peaks the arrangement of a molecule can be worked out.

And the symmetry of each structure, with its spatial array of groups has a beauty of its own, tensile and strong. Energy efficient.

So that's one part of the picture.

The brain, representative of the powerhouse of cerebral activity, is another.

For it translates, cross links and multiprocesses several chunks of this kind of arcane, disparate information.



Eventually creating a product that touches human life. Causing a human connect.

A connect that places almost a magical spell on the demanding discipline of drug discovery. Transforming lives. At the close of an interesting year, the domestic pharma market registered a 6% growth rate, and had quietly been settling towards this number for much of the year. Large volume segments such as antibiotics continued to register slower growth on account of increased price based competition. Despite some instances of the entry of lower priced speciality products, such as lower priced fluoxetine brands, atorvastatin or celecoxib brands, the higher end speciality therapy areas continued to show a double-digit rate of growth.

At Sun Pharma, formulations (domestic and exports) were the drivers of growth for the year. As every year, SPARC helped bring several interesting products to market, several of these such as the prostrate cancer treatment Lupride Depot and the asthma inhaler range Sunhaler, used technology for a differentiating advantage. High margin complex bulk actives were also developed and scaled up. Several of these enabled us to be the first to market with an interesting formulation.

Keeping in mind the tremendous opportunity in global markets, the work we've done so far represents a beginning, yet a modest one, since we still have to go a long way keeping in mind the opportunity upside ahead of us. We now have an on the ground presence with products registered and a good pipeline with products under registration. After a confident double digit growth number in the exports market this year, we aim for a similar number for the next year too.

In the Indian prescription product market for March 03, Sun Pharma this year stood firm at 5th rank, the same position that we've been ranked at, for the last two years. Overall prescription share improved significantly. The AC Nielsen-ORG Retail Chemist Audit









March 03 shows a 15% growth rate for the company as versus 5.4% for the industry. Market share is strong at 2.99%, up from 2.8% last March, reflective of the increased prescription share in each of our therapy areas.

On the C-MARC audit, prescription share moved from 2.0% to 2.1% and we were amongst only two companies to increase market share in the top 10 companies listed there.

In core therapy areas, ranks were maintained despite increasing competitive interest. In select non-core therapy areas such as oncology and gynecology, in which we hold a long-term interest, dramatic rank increases were seen. We continue to seek means to put in place customer relationships in these new therapy areas, for at the end of the day, customer trust is the differentiating factor between a top rank and an also ran.

The most apt backing for the numbers was from the C-MARC doctor audit, with diabetology also featuring among therapy areas where we rank among the top 3- which in effect now takes the total number of such core therapy areas, to 5. Diabetology, a high prestige therapy area for the company entered the top 3 rankings after 5 years of effort, despite the fact that we do not market an insulin range, a staple of a large chunk of prescriptions that are written for diabetics.

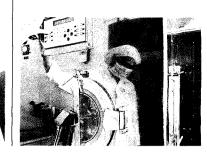
The 5 core areas: psychiatry, neurology, cardiology, diabetology, gastroenterology accounted for over 72% of domestic prescription formulation sales. 6 brands continued to feature in the list of the top 300 brands as per the ORG. In keeping with our record of aggressive new product introductions, interesting new products were launched including 16 with a different technology or complexity of formulation. At the close of the year, over 100 products were among the top 3 by molecule, signalling the growing strength of the product basket.

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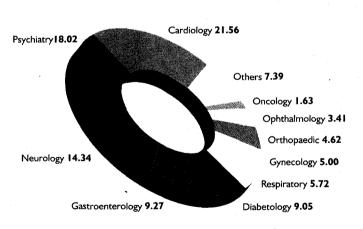




getting better managed as we learn how to manage logistics and construction challenges in different kinds of terrain.

Turnover for 2003 was up 15%, backed by a 24% growth in domestic formulations, and 40% growth in international formulations. Among top runners in the domestic market on performance were Synergy, Symbiosis, Arian and Inca divisions, rated on target achievement of fairly stiff, high stretch numbers.

In order to meet anticipated increases in domestic market demand as well as in order to be able to source different types of formulations in house, an additional facility in Jammu is being built to comply with USFDA and UK MCA norms. This 9500 sq. ft built up area formulations site, created to meet international regulatory standards, is expected to be operational early next year. Like most Sun Pharma projects, this site too, was made operational in record time, with tight schedules. Over the years, these schedules are Dosage form exports now begin to live up to their promise. The speciality strategy that we've perfected with great success in the Indian market is the same one that we are putting into place in the international market, and given the fact that most these markets have much larger speciality segments than we have in India, we expect the pickup to be that much quicker. The turnaround we've seen this year is on account of the proper execution of strategy on the ground. With the manpower and resources not vastly different from that in the past, and with 200 people on the ground in 36 markets, we now have in place a well-entrenched base that we shall now build on. We believe this is only a better or more sensible allocation of resources that we had in any event put to work earlier, however going ahead we certainly expect to increase the spend. The international formulations business is likely to grow much faster over the next few years.



	(Rs. Mill)		
Sales Breakup by type	Mar 03	Mar 02	
Domestic Formulations	5764	4661	
Domestic Bulk	1335	1398	
Others	19	23	
Export Formulations	398	284	
Export Bulk	1062	1070	
Export Others	9	42	

THERAPY WISE BREAK-UP (%)



Plant 2, Nagar

Across domestic and export markets, the turnover of speciality bulk actives was Rs2397mill, or 28% sales. After we phased out cephalexin bulk actives completely and replaced this with better margin speciality bulk, which is sold largely to end users in the regulated markets, the margins for the bulk business have improved remarkably. 5 high value bulk actives were scaled up and introduced this year, and most critical of all, during the year 3 more DMF and 3 COS were received, and we also received our first Australian TGA approval for bulk actives.

The USFDA approved Ahmednagar plant received 3 more DMF approvals, taking the total DMF approvals from this plant to 4. Panoli received 2 more bulk approvals for Europe for COS, taking the tally now to 3. Both plants have been routinely inspected during the course of the year by a number of international companies as a part of their site registration process. The facilities at Ankleshwar and Chennai received ISO 9002 certification during the year. The Vapi formulation plant also received ISO 9002 approval.

As we've indicated, Ahmednagar and Panoli plants are now largely dedicated for the international regulated markets, and the other two bulk plants, Chennai and Ankleshwar, are meant for India and the neighboring markets.

We anticipate reaching good numbers with speciality bulk actives in these markets as we consolidate this business and develop long-term customer relationships.

A discussion of the key marketing divisions follows

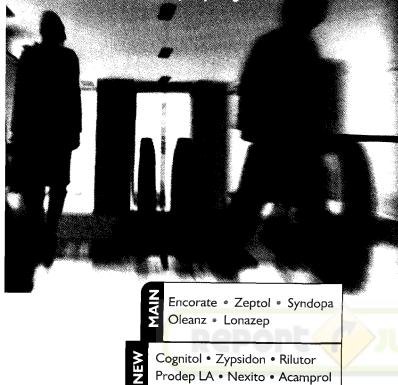
Product processing, Panoli	
" v in	

Sun	262	Milmet	95
Spectra	257	Symbiosis	85
Solares	257	Inca	76
Arian	167	Radiant	73
Aztec	167	∞ RTF	30
Synergy	99		

C-MARC			
	JULY 01 TO OCT 01	NOV 01 TO FEB 02	NOV 02 TO FEB 03
Psychiatrists		I	. 1
Neurologists		I	ł
 Cardiologists 	, 4	3	3
Gastroenterologists	2	3	3
Chest Physicians	6	4	4
Consultant Physicians	6	8	5
Orthopedics	4	6	6
Ophthalmologists	4	4	4
ENT Specialists	5.	5	5 · ·
Diabetologists	6	6	3
Oncologists	II ·	7	6
Nephrologists	8	8	8
General Practitioners	22	23	22
Pediatricians	33	34	49
Surgeons	23	21	16
Gynaecologists	17	17 .	

SYNERGY

The hustle and bustle of daily living 24/7/365 exacts its toll



Increasing lifestyle related reasons, the stress and demands and choices of modern living have meant that these sectors like psychiatry and neurology continue to be high growth. This is regardless of competitive pressures or the state of the economy, that tends to affect other large volume therapy areas. As the largest player and the company most often associated with this therapy area, the division continued to partake of most of this growth.

Competitive interest is not remarkably greater than what we've witnessed in the previous two years, when we first saw the influx of companies that earlier used to compete in the large volume part of the business, stalwarts with deep pockets and an abiding interest. The nature of the competition has changed to one that is much more serious, and intent on the long term - companies that have a better grasp of the market and ground realities. We now appear to be in the period beyond the shakeout- the first bout of price-based competition is past us, and the ones that remain have got what it takes. However, its to the division's credit and perception with its customer group that it continues to add to prescription share despite the presence of these larger companies.

Battling the scourge of alcohol dependence



Fine dining?

Alcoholism places an enormous burden on Indian society. What makes it worse is that as a health problem, addiction remains unrecognized although it strains the economy, rips apart family life and endangers public safety.

Alcohol abuse crosses all societal boundaries, affects both genders, and people at all income levels. The jury is out on the why's and whereforesscientific documentation indicates alcoholism has roots in the gene makeup as well as traits in personal behavior.

This is a global problem. It is estimated that in the US, one-quarter of all emergency room admissions, one-third of all suicides, and more than half of all homicides and incidents of domestic violence are alcohol-related. Heavy drinking contributes to illness in each of the top three causes of death: heart disease, cancer and stroke.

Almost half of all traffic fatalities are alcohol-related.

Alcoholism is treatable and thousands of people achieve recovery. Chronic exposure to alcohol causes a decrease in the inhibitory neurotransmitter called GABA in the brain, and an increase in excitatory neurotransmitter.

Acamposate, the medication in Acamprol has a similar structure to this neurotransmitter GABA, and enhances GABA transmission in the brain

Mind the Label 'Mental'

I note that the writer calls depression a mental illness.... Do we commonly call pancreatitis a digestive illness, or pneumonia a respiratory illness?

No. They, like depression, are simply illnesses. The retention of the term "mental" sustains stigma, supports resistance... It is time to acknowledge that depression -- and mania and schizophrenia -- are just as physical as any other illness.

(From a letter written to the Editor, The New York Times)





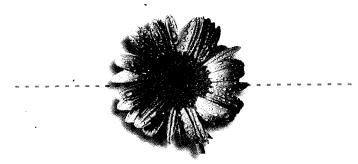
Antiepileptics continued to be the fastest growing among Synergy's therapy areas, followed by Antidepressants, where products that were 2 decade old, like Amixide, continued to gain prescriber support. New indications also continued to expand- such as the use of gabapentin in the treatment of restless legs syndrome, as well as hot flashes in post menopausal women, to name just a few indications being studied.



In Parkinson's, an important area for this division, new treatment guidelines were issued, offering first use preference to dopamine agonists such as Amantidine. Ropinirole, the medication in Ropark also received a boost with the publication of a 5 year study which showed that beginning treatment first with this medication instead of levodopa, or adding levodopa as a supplement helped to delay the loss of muscle movement in Parkinson's.

Riluzole, the medication in Rilutor, is used for the treatment of a neurological ailment associated with muscle wasting - amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease). In certain trials riluzole helped delay the loss of muscle strength. As a patient care service, Rilutor is being provided entirely free to patients who have a valid prescription for the same.

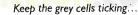
New guidelines for bipolar mood disorder were also published, advocating the use of atypical antipsychotics such as Zypsidon to treat the manic part of the episode, and other antiepileptics, to handle the depressive downswing- hence handling both the extremes of this illness.

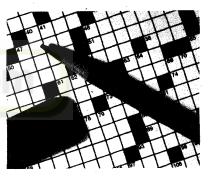


Two important additions to Synergy's therapy offering for depression were made this year with the introduction of a once-a-week, delayed release formulation of the time tested antidepressant fluoxetine, Prodep LA. Fluoxetine's uses have been expanded greatly-in addition to the approved uses in depression, panic disorders, OCD, eating disorders, off-label uses have been shown in diabetic neuropathy, migraine, depression accompanying premenstrual syndrome, HIV...

Nexito, a formulation of escitalopram was also launched to a fairly good success. Escitalopram is the purer, single isomer only form of the earlier antidepressant Citalopram, and appears to require lesser dosing, an advantage. In studies, 10 mg of escitalopram were shown to be as effective as 40 mg of citalopram.

The case for longer depression treatments-ongoing treatments rather than episodic received a shot in the arm with the publication of a review of 30 years of studies in the Lancet. While doctors treat depression as an episode, it is more often than not likely to recur, in as many as 4 of 5 patients. Most patients should continue taking medication after their gloom has lifted, this research suggests. In this analysis by researchers at Oxford University in England, patients who stayed on antidepressants were half as likely to have another bout of depression as those who stopped taking medication.





A prescription to keep **memory loss** at bay

Crosswords, Quizzes, reading or scrabble may just be the right prescription to keep the brain ticking and mentally on the go, ticking near capacity regardless of age. Studies reported in Neurology and JAMA point to a need for mental activity, the more the better.

A beginning was made in an important but less understood disease area- Alzheimer's - with the introduction of Cognitol (vinpocetine). Identifying the triggers for this mind numbing disease, in one of the largest studies involving the medical records of World War II



veterans, a linkage was seen between head injury and Alzheimer's, with people who had severe head injury four times as likely to develop Alzheimer's - how far this could apply to other injuries better identified with modern living, is not as yet, known. Several studies looked at the link between diet and Alzheimer's - and specifically in people at risk because of a genetic variant, who may benefit by opting for more balanced diets that limit saturated fats, and cause less damage by free radicals rather than high-calorie, high-fat diets. In another study, researchers showed that it was possible to use visual memory tests to identify people at risk for Alzheimer's very early, much before the degradation of dementia set in.

An artist's depiction of the hues of mania- restful blue dipping to raging red

An important atypical antipsychotic was introduced with Zypsidon (ziprasidone). Ziprasidone improves both positive and negative manifestations in acute exacerbations of schizophrenia and reduces the rate of relapse compared to older antipsychotics. This class of antipsychotics is free of interfering side effects like dry mouth, stiffness and trembling, and patients are therefore likely to continue taking their medication. Older medication while effective at handling the outages had problems such as emotional blunting, a typical dull eyed stare, stiff legged walk, withdrawal and depression. With the older medication, repetitive chewing action, lip smacking, contortions of the arms and legs - a bundle of symptoms grouped under the term "tardive dyskinesia" were a serious interfering problem. In schizophrenia, the thumb rule is that by the end of 2 years, 75% of the patients are not taking their medicines, and more often than not, this is part of a logic that says, "if I don't take medication, that proves I don't have the illness." But after some time of no medication, relapses occur, and these can be terrifying, such as hearing voices and being unable to distinguish make-believe from reality. Each relapse takes something from the patient, leaving them with a harder climb back to normalcy.

Just the blues?

Depression, condensed

"People are making it to work, They're just not engaged in work. They're getting to the door, but then closing it and just not functioning. People have called this "presenteeism", and it is often invisible to employers."

A New York Times, June 18, 2003 report "More Americans seek treatment for depression", quotes 16% of the population as suffering from depression that requires treatment at some time in their lives, or 6.6% of the US population in a single year. General practitioners are not geared to treat this adequately- at times patients were given a quarter of the prescribed antidepressant dose. That depression strikes so early in life, makes it a vital health problem. Hypertension and arthritis start at age 55-Depression starts at 15 or 25. So the number of years of suffering in a person's life is much higher. And at significant risk is the medical community itself, with doctors showing a higher propensity to suicide than the general population.

Reporting in the Journal of Occupational Health and Psychology, Richard Price of the University of Michigan says that not just job loss but a prolonged cascade of events keeps a person in an extended state of depression... with a fallout even 2 years after job loss... these people become discouraged workers, not searching for a job, with high personal, family and societal costs...

These post job loss events may spiral into disadvantages that reduce life chances even further.

(Reuters, Oct 8, 2002)



Amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease, is a progressive, fatal neurological disease. The disorder belongs to a class of disorders known as motor neuron disease. ALS occurs when specific nerve cells in the brain and spinal cord that control voluntary movement gradually degenerate. The loss of these motor neurons causes the muscles under their control to weaken and waste away, leading to paralysis. ALS manifests itself in different ways, depending on which muscles weaken first. Symptoms may include tripping and falling, loss of motor control in hands and arms, difficulty speaking, swallowing and/or breathing, persistent fatigue, and twitching and cramping, sometimes quite severely. ALS strikes in mid-life. Men are about one-and-a-half times more likely to have the disease as women. Riluzole, the medication in Rilutor is the first drug that has been shown to prolong the survival of ALS patients.