JKS READING ROOM

Measuring the intangible

(Market Research in Japan)

Measuring the intangible

LICENSCAPE
Market Research, Japan

Cultural idiosyncracies and regulatory restraints that have crippled the Japanese pharmaceutical market for decades are unraveling. Could an innovative approach to pharmaceutical market research play a new role in the changing environment for drug development in Japan?

Monitored for years, the size of the Japanese pharmaceutical market remains the second largest single country market after US, and of relatively similar size compared to the five leading EU economies of Germany, UK, France, Spain, and Italy. What makes this market unique? Aside from the measurable factors of R&D expenditure, insurance coverage and pricing and reimbursement controls, a number of intangible factors stemming from customs, culture and traditional beliefs affect not only the sales of medicinal products, but drug discovery and development as well. This article will explore how innovative approaches to drug market research could significantly influence Japanese product development, clinical trials and marketing.

The *yakuji*

Until the late 1990s y*akuji* (pharmaceutical affairs in Japanese) was distinctly different than that of many other, especially industrialized, countries. Placed under strict governmental control in 1961, the heavily-protected yakuji grew to become self-sufficient, non-tariff guarded and uncompetitive. By the late 1980s the number of pharmaceuticals registered in Japan, but not approved in any other country reached its maximum. Perhaps the worst example was picibanil. Manufactured by Chugai Pharmaceuticals and given to virtually every domestic cancer patient, it was not only not approved, but never even submitted overseas. Such omnipotent drugs were in the hands of equally omnipotent *sensei* (doctors) practicing with an unquestioned authority. Their paternalistic attitude to the patients was not only a matter of tradition or personal style, it was legally stipulated. Clinical trials were conducted without patients' consent, doctors were free to both prescribe and dispense, and under no circumstances could patients or their families get access to medical records.

Towards a change

However, the seemingly unbreakable triad of regulatory protectionism, untouchable doctors and voiceless patients started to crack along with the larger economical tendencies by the end of the 20th century. Firstly, pressed by international dismay and escalating internal criticism, the regulatory authorities introduced a system for stricter re-evaluation of the already approved drugs, as a result of which many of the Japan-only products were either disapproved or re-approved for a seriously limited number of indications. In parallel, Japan started to integrate its regulatory requirements by joining, in 1990, the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use as a founding party and introducing new Japanese Good Clinical Practice regulations in 1997. Next, data included in the clinical data packages used in foreign countries became acceptable in Japan, and results generated in bridging studies became admissible. Thus the whole process of reviewing and approving new drug applications was streamlined and shortened. Most recently, some new chemical entities such as Iressa (gefinitib) received their first international approval in Japan. Furthermore, on April 1, 2005 the most significant amendment of the key pharmaceutical statute of Japan since 1961, the Pharmaceutical Affairs Law, will be enacted. As a result, the regulatory authorities will be re-reorganized into a new body and the outdated dual system of *Shonin* and *Kyoka* will be turned into a single approval procedure similar to that of the MAA in EU. The most foreseeable consequences would enable domestic makers to outsource active substance production and facilitate access to Japan for foreign companies, particularly manufacturers of innovative therapeutics and quality generics.

Meanwhile, changes have occurred in the doctors' practice too. The government is finalizing the separation of prescribing from dispensing. In clinical trials, physicians have to comply with GCP requirements and site management is becoming more transparent. The relationship between sponsors, CROs and investigators is being scrutinized more than ever. In addition, not only is informed consent for participation in trials obligatory,

Japanese mini-glossary

Yakuji	Pharmaceutical affairs, issues
Shonin	Manufacturing and import approval
Kyoka	Manufacturing and import license
Giri	Sense of obligation, specifically to a benefactor
Keigo	Way of speaking employing an extensive system of politeness and honorific markers
Sensei	Doctor, teacher

but patients have also succeeded in obtaining much wider access to their medical records and other previously off-limits information as a consequence of The Law Concerning the Access to Information Held by Administrative Authorities enforced in 2001 and unrestricted use of internet. A recent survey (See Fact finding box) found mushrooming Japanese language websites featuring migraine, headache and depression, topics until recently considered unfit for public discussion. Patient support groups for sufferers of other 'shameful' conditions such as sexually transmitted diseases are also becoming more vocal in print and online.

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Attitude matters

First launched in US in 1988, Prozac is expected to be approved in Japan later this year. However the 17-year hiatus was not the result of regulatory or research hurdles faced by Lilly Japan. While commercially aware of the large number of mild-to-moderate depression cases, as late as 2000 the company did not pursue registration in Japan assuming that the profound cultural stigma against mental disorders would compromise the prescription volume. Except for cases of acute psychoses and severe retardation, anything else related to the CNS was perceived not only by the general public, but by a sizable part of the medical community, as a character flaw or lack of willpower, and thus treatable by self-control or rest. The belief among drug developers that the attitude of the Japanese patients will not change has delayed and even prevented domestic introduction of key medicines.

For years, the power of the public attitude has influenced the drug development in another way too. Once accepted by the makers that both doctors and their patients would resist generics, the introduction to the market of cheaper alternatives has been delayed, or simply not pursued, until recently. The affluent Japanese are perhaps one of the most brand-conscious and had pharma companies been allowed, they would have opened fancy downtown shops no less successful than the most profitable Louis Vuitton outlets in Japan. The effect of this cultural attitude on drug development has also been seen with physicians. Due to a typical Japanese *giri* sense of obligation, a doctor involved in some way with one pharma company not only would not participate in a competitive clinical trial, but also would simply refuse even to talk with representatives from a different developer.

Pharmaceutical market research

Two key questions are anticipated to be increasingly posed in the future. First, is market research able to gauge trends in a market as insular as the Japanese? Second, can contemporary and methodologically advanced market research play a significant role in the R&D process for medicinal products? The answer to the latter question is positive but conditional, as long as the current trends in changing prescribers' attitude and patient

Fact finding

Original research - as of February 2004, a total of 3850 web sites were retrieved on a major search engine by using the Japanese word for triptan, and 1750 hits were yielded for the Japanese term for migraine.

Original research - a total of 65 market research entities (both domestic and affiliates of foreign entities) were analyzed according to the following criteria: self-description as market research business and self-declared as capable for pharmaceutical (medical, healthcare) market research. Approximately 30% of the entities surveyed were found to have declared in their print or online promotional materials as being capable of healthcare (medical, pharmaceutical, etc) market research.

awareness are maintained and bold steps continue to be taken by the authorities toward deregulation.

Until recently, prescriptional pharmaceutical market research was a niche in an otherwise billion dollar industry in Japan (estimated to be US $1.07 billion in 2001: source, ESOMAR). As a whole, the market research industry in Japan lags behind the other industrialized countries, accounting for around 0.03% of the GDP expenditures compared to 0.06% in USA and 1.2 % in UK.

A comprehensive survey (see Fact finding box) on the disclosed activities of 65 firms found that nearly one third included medical market research in their services. Further breakdown of the activities however, revealed that along with the capabilities for conducting research on prescription medicines and OTC products, experience with consumer health and even with pet care products was included. After sifting these out, the number of research firms with confirmed capabilities in Rx/OTC field the number fell to less than a dozen. The second stage of the survey (face-to-face interviews) explored whether those outlets with denoted capabilities could organize, conduct and analyze primary research projects targeting all parties involved with prescription, reimbursement and consumption of prescription medicines. The survey found that few of the covered firms have experience in this area.

The respondents largely fell into three groups: (i) companies having actual experience including maintaining of databases with eligible physicians and/or patients; (ii) firms having certain capacity for Rx market research, but as a rule outsourcing the job, and (iii) outlets stating "capable of medical market research" for promotion, but in fact without any experience of such projects. Furthermore, the majority of participants from groups (ii) and (iii) regarded the Rx market research not only as difficult, but also expensive and frustrating. Having conducted research predominantly focused on self-medication and consumer health products for years, these companies face daunting difficulties. As one executive put it: "It is much nicer to conduct research on a new skin-whitening cream than on a product for skin cancer."

Good market research allows drug companies to understand Japanese culture and orient new products accordingly.

Most of the firms are understaffed and underqualified when comes to pharmaceutical issues and all were concerned with their capacity to monitor and interpret relevant regulatory affairs. Additional problems included the difficulty of 'handling' time-pressed doctors, preparation of questionnaires and analysis of answers (particularly those containing terminology), and the cultural and scientific adjustment for both the study and the results in the cases of international projects. Further diminishing the attractiveness of Rx research are the increasingly higher standards for privacy, and determining and applying incentives in a country where all patients are health-insured.

A formidable challenge lies in the process of 'to and from' translating - most often from English to Japanese - of the original material like questionnaires,

Case study A

In a Japanese research project on innovative therapy for certain genital neoplastic formations, a questionnaire prepared for other concurrently surveyed regions (EU, North America) was used, together with an invitation letter that had been translated into Japanese. Due to the sensitivity of the conditions for both the physicians and the patients, all the documents needed to be prepared in careful and highly respectful language. However, while both the texts were scientifically accurate and stylistically very reasonably polite, the translation to Japanese stumbled into an unusual occurrence. The invitation letter started with 'Dear Doctor, You are invited…' and went to contain 22 mentions of 'you' thought the text. Worse, the leading researcher and author of the letter repeatedly used 'I' when addressing the doctor. Neither 'I' nor 'you' are acceptable in the *keigo* – the polite Japanese language supposed to be used in such occasions. The attempts to translate to Japanese while omitting 'I' and substituting 'you' led to such an awkward version that it was decided simply to re-write the texts.

Case study B

A maker of a novel medicinal product designed to deliver faster and longer-lasting relief of headache wanted to find out whether the product might compete in a market saturated with both classic analgesics and newer medicines. If approved, the product was projected to fetch a reimbursement price in a range comparable with already registered products. The maker was interested in whether the physicians would be willing to switch from the prescribing routine to a new product. However, the original questionnaire, while designed well in English to differentiate between various forms of cephalgia, somewhat poorly related to both the adopted classification of the diseases in Japan and the layperson's understanding of the nuances of headache, pressure and lightness. This prompted a mini-study preceding the main study. The objectives were to verify both the equivalency of the medical classifications (Japanese and Western) and consensus among the patients regarding their conditions, the verbal expressions and even the image conveyed by the Chinese characters used when self-determining the episodes of pain and relief. Once the mini-study confirmed that there was a clear, reproducible way to translate the original questionnaire to Japanese and then to convey correctly the answers back to English in both a linguistically and scientifically correct manner, the main research study was commenced and completed successfully.

screeners, invitation letters, etc, and back into English of outputs such as answers or comments. While the Japanese language permits a translation true to the letter of the original in all cases, this cannot be said for the spirit of the documents (Case study A).

Expectations

The perceived high barrier for entering Rx market research however, appeared to be a problem at those firms bound to legacy concepts and established routines in less challenging segments of market research. In a quite opposite way, Licenscape was founded not just to extend the more traditional market research into prescription area, but to offer services and expertise matching the highly specialized level of Rx research. The founders' medical/pharmaceutical and communication backgrounds offer two key advantages: a combined incentive- and merit-driven recruitment technique and proprietary interviewing methodology that blends elements of contemporary market techniques with diagnosing approaches used in medical practice.

The recruitment process for both doctors and patients has always been a challenge in Japan. Convincing the 'front-line' general practitioners unused to interviews and the level of publicity the market research studies may create is not easy. Neither is providing the time-pressed key opinion leaders, to whom the financial incentives may not be meaningful, with reasons to participate. Yet defining the right incentive for participating for both medical professionals and patients appears to be the key for a successful recruitment. One core element of the interviewing methodology is the proper use of the Anatomical, Therapeutic, Chemical Classification System and New Form Code Classification System, paired with proprietary glossaries developed in-house by Licenscape. This quality assurance step provides scientific and linguistic consistency when the objectives of the study are translated into Japanese, and accurate presentation of results in English. As described in Case study B, had the foreign pharma company been pre-convinced that due to the linguistic differences no meaningful results could be obtained or worse, been misled by erroneously interpreted answers, its product would have never be submitted and successfully registered in Japan.

Reliable decisions

A well planned, professionally executed and objectively interpreted marketing study will help companies predict market positioning of new products, provide information on competitors, elucidate potential obstacles and calculate estimated revenues. New legislation scheduled for spring 2005 will provide an incentive for foreign companies to set up in Japan. Judging by the increased amount of market research being conducted, entrants onto the market will be well prepared.

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FURTHER INFORMATION

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www.mhlw.go.jp

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