Key R&D informatics challenges facing small/medium-sized pharmaceutical and biotech companies

The ability of R&D informatics to deliver real benefit to the SME pharmaceutical company is constrained by the increasing burden of non-discretionary computer systems combined with the lack of opportunity to leverage the economies of scale enjoyed by the large pharmaceutical companies. Furthermore, the relationship between R&D informatics and the corporate IT department still continues to display some elements of misunderstanding. This paper attempts to identify an alternative way such that SMEs might gain the advantages of economies of scale and enjoy the benefits of working with customer-facing organisations by exploiting the increasingly rich offerings available from ASP-based solutions providers.

By John Wise

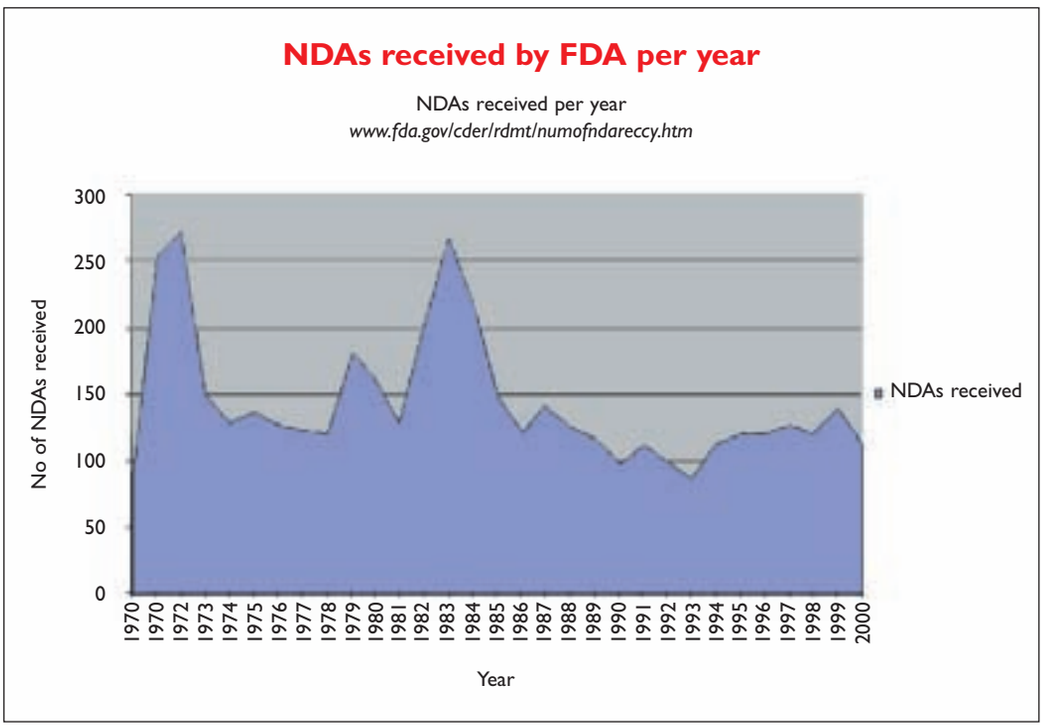
Derived from data published on the FDA website, **Figure 1** is a graphic but simple metric that shows that the pharmaceutical industry has failed to increase its capability to deliver NDAs to the FDA. The developments in science and technology over the past 30 years have not been successfully exploited by the industry in its quest for more new and innovative medicines.

Despite the substantial investment in computer-based technologies made by big pharma, it is only just being able to keep pace with the quantity of information that it has to process in order to deliver NDAs. If big pharma cannot manage, what hope is there for the SME[1]?

"The move towards e-R&D – the computerisation of the R&D process – is partly a response to greater financial pressures as well as a consequence of advances in chemistry, biology, computing, automation and pharmacogenomics. Yet most pharma companies are ill-equipped to make the transition partly because their IT is underfunded and overworked."[2]

The e-R&D domains and the R&D informatics[3] portfolio required to support them is much the same in the SME multi-national pharmaceutical companies as in big pharma (**Figure 2**). If e-R&D is underfunded in big pharma with its opportunities to leverage economies of scale, such underfunding

Figure 1



must be felt more acutely by the SME. Consequently, simply copying the e-R&D paradigm of big pharma – albeit on a smaller scale – will not produce an optimally e-enabled SME.

Why is R&D informatics underfunded and overworked?

Many factors contribute to the costs of informatics; the rapid spread of informatics into all parts of the value chain, the plethora of competing products and systems providing too much diversity, technologies becoming rapidly obsolete, the shortage of informaticians forcing up salary bills – all these contribute. But the reason for underfunding must lie with those with ultimate responsibility for the development and deployment of informatics within the pharmaceutical industry. Many functional informatics groups exist supporting the pharmaceutical industry value chain; R&D informatics is an example. There are also IT functions within the affiliate company structures. But most, if not all of these IT organisations have a relationship and a reporting line to the corporate IT function.

Corporate IT

Historically, corporate IT has assumed many responsibilities: some soundly based, some less securely so. Setting IT standards to decrease diversification of equipment and software is clearly sensible (if sensibly organised). Such standards significantly increase the computer-based communication capabilities of a company and also drives down computer-based expenditures – especially in the area of support and maintenance where diversification drives up manpower requirements and thereby costs.

Corporate IT has also had considerable influence in determining the amount of informatics investment made within the company as a whole. Such decisions have often been largely based on comparison with industry benchmarks of informatics spend as a function of sales, rather than of a business's clearly determined need. These benchmarks are notoriously difficult to calculate, the margins of error are high and the value of these comparisons often dubious.

If the ultimate responsibility for informatics expenditure lies with corporate IT, where does corporate IT report? In many organisations it reports to the finance directorate.

The origins of this reporting line are clear – back in the infancy of computer usage, computers were machines that were quickly adopted to help finance people to calculate finances. Finance people control finance and therefore they controlled the computers too. Unfortunately, here lie some of the seeds of misunderstanding of the role of computing within the organisation. In parallel with this development of computing within finance was the development of computing within the research laboratory and

the contrast between these two domains could not be sharper. The former is by nature conservative; the latter by definition is innovative, exploratory and adventurous. I wrote in 1997, "…the pharmaceutical industry has been slow to accept the need for management focus on Information Technology in Research & Development and, in general, has been content to let IT be directed from the office of the Finance Controller."[4] Plus ça change, plus c'est la même chose!

Informatics is ubiquitous

Computer-based technologies are now exploited almost everywhere. Is it still within the capability of the Finance Director to give proper attention to this ubiquitous technology? At boardroom level, informatics is portrayed as a cost rather than being seen as a source of competitive advantage. Measures are taken to control cost rather than initiatives launched to exploit this capability. The pharmaceutical company that does not have a CIO[5] operating at board level is a company that may be failing adequately to exploit informatics to maximise the effectiveness of the drug development processes.

Informatics as a cost or a source of competitive advantage – ROI

To compound these problems, over simplistic models have often been used to calculate the benefits returned from investment in informatics. Some aspects of an informatics project may produce "tangible benefits which will directly improve the performance of the firm, such as reducing costs, and will therefore be seen in the accounts of the organisation as an improvement in profit and perhaps in return on investment (ROI)."[6]

However intangible, benefits can make a critical contribution to the success of an organisation but self evidently are less easy to measure in the accounts. Eg a decision support system, used during clinical candidate selection, could provide enormous benefit to an SME if it increased the accuracy with which potent, drug-like entities with good ADME/Tox[7] profiles were selected. This would minimise the enormous drain on the organisation caused by developing

Figure 2

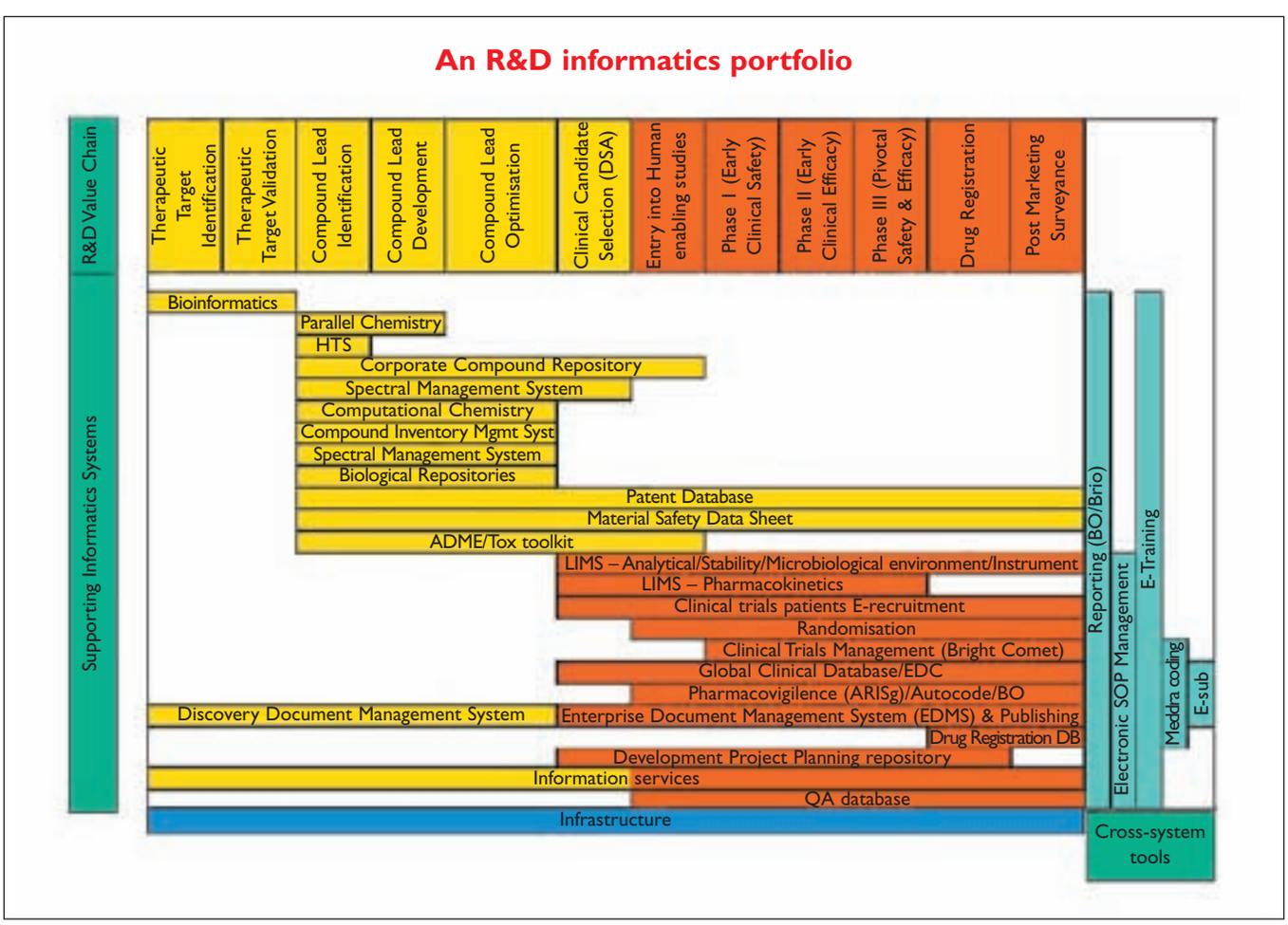
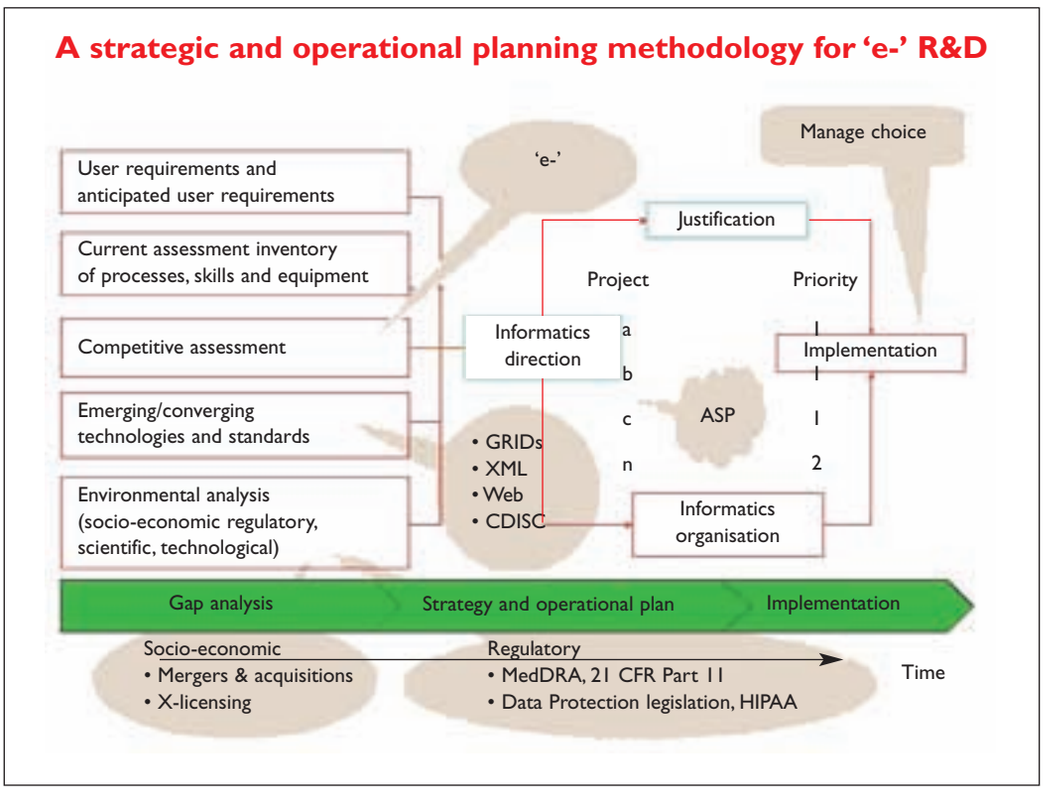


Figure 3



compounds that were in fact doomed to failure, later on in the more expensive phases of clinical trials, due to poor human ADME/Tox profiles.

The challenge for management is to invert its thinking about informatics. It should not be seen as a cost but as a source of competitive advantage. The catalyst to bring about this change is a plan for informatics. The activation energy is to consult representatives from across the organisation; to involve them in the planning process.

'e-' planning

One of the difficulties faced by the SME pharmaceutical company is how to set out in a clear way – for both users and management to understand – the informatics challenges it faces. A crucial part of this challenge is to make sensible choices, from the many possibilities of appropriate systems and services to support the business, that collectively provide a state-of-the-art informatics environment. The SME requires a process that defines the problems, elaborates and chooses the solutions – with the general acceptance of all the stakeholders. This process can be called providing a consensus-based strategic and operational plan for 'e-'[8].

A strategic and operational plan for 'e-' within the SME must reflect and support the strategy and business objectives of the SME. It is not uncommon, within any sized organisation, to find these key directions poorly communicated and hence not clearly understood by the organisation at large. Indeed, the activity of producing such a plan for 'e-' can provide an excellent vehicle for reinforcing the communication of company strategy and business objectives to the organisation.

Planning methodology

Figure 3[9] attempts to depict some of the major activities required to derive a plan for 'e-'. Most importantly, the information needs to be gathered with wide consultation within the organisation. Nowadays, information technologies are so widely deployed within organisations that many different stakeholders believe (often rightly) that they have a contribution to the thinking about informatics; few sustain the belief that corporate IT by itself has a unique wisdom in identifying how informatics should best be deployed.

The following paragraphs contain a high level description of the components of the planning methodology. The topics depicted on the left hand side of the diagram are used to assess the needs of, and the capability for, 'e-'based activities within the organisation. The 'gap analysis' compares them with competitive capabilities as well as emerging business, regulatory and technology trends, documents the deviation from the desired path and leads to the determination of an informatics direction to remedy the deficiencies.

User requirements
By running workshops and distributing questionnaires, the SME strategic direction can be communicated and informatics needs ascertained. By exploring the minutes of informatics users groups meetings common complaints can be discerned.

Current inventory
Creating an up-to-date inventory of informatics systems enables insight into the current capability and cost of informatics and the ratio of budget expended on maintenance compared to budget expended on investment. This also provides an excellent opportunity to assess the skills of the R&D informaticians.

Competitive assessment
A high level awareness of informatics activities in competitive or comparable organisations allows one to 'benchmark' one's own company's position. Such activities broaden the perspective of the organisation towards informatics and decrease the pharmaceutical industry's inherent tendencies towards parochialism. Consultancies can be particularly useful in such activities and a good example of this is provided by a recent study by David Hardison of FCG[10] comparing the uses of informatics in clinical development across a large representation from big pharma and some CROs.

Emerging/converging technologies/standards
Constant attention to technology trends is essential to minimise the disadvantages of getting stuck with obsolete systems and the costs of disengaging from them. Regulatory 'hurdles' such as 21 CFR Part 11 can be a significant shock to organisations that have allowed themselves to become encumbered with obsolete systems. Emerging industry standards, eg E2B, CDISC, MedDRA must be tracked and implemented when endorsed.

Environmental trends
Regulatory: MedDRA, 21 CFR Part 11, HIPAA and other patient information privacy legislation – technically very difficult – use experts.
Staffing: Decreasing availability of fully skilled and experienced R&D informaticians (with communications, domain, informatics and project management expertise).

Gap analysis
From analysis of the information obtained, it will become clear where the user requirements are not met by the current inventory of informatics systems, where the competition is forging ahead in informatics developments and where potentially useful technologies are not being tracked or exploited. Furthermore, the increasing burden of the regulatory authorities on the day-to-day activities of informatics supporting the regulatory domain of the SME will become apparent. The documentation of this 'gap analysis' will allow an informatics direction to be determined.

Informatics direction
Here the major thrust for informatics in its challenge to support the business can be defined. For the SME in today's environment the direction will be in general towards 'e-' and in particular towards Application Service Provider (ASP)-delivered solutions. For example, in a recent paper[11] Carol Farina, the CEO and Managing Director of NiKem Research in Milan, described how he had provided his research centre's entire informatics service using an ASP model delivered by Getronics.

Justification
In this section, the rationale of the informatics direction and its underlying organisation can be addressed. Appropriate financial or other business returns of the project portfolio can be assessed and described, eg a detailed analysis of the costs of supplying solutions via ASPs compared to constructing them in-house.

Informatics organisation
Here the proposed informatics organisation, optimally designed best to support the business, can be described.

Implementation
The project portfolio will need to be assessed in terms of priority for undoubtedly there will be more projects to implement than resources available to implement them. Priority can be assigned to projects in terms of the benefits they bring to the organisation, the risks in implementing them and the effort needed to be expended.

Benefit can be calculated in many ways. A financial approach might use metrics such as Payback, ROI[12], NPV[13], IRR[14] or opportunity costs. A customer satisfaction approach might consider increased utilisation of a system or enhanced capabilities and speed in customer support. A decision support approach might attempt to estimate speed and accuracy of decision making.

The calculation of risk is dependent on many variables too. Technical complexity, interruption to, and modification of, business processes, the culture of the organisation towards change, user commitment and geographical spread, are all examples and need to be combined in an understandable way to provide a risk quotient.

The projects need to be assessed relative to one another, according to risk, benefit and effort

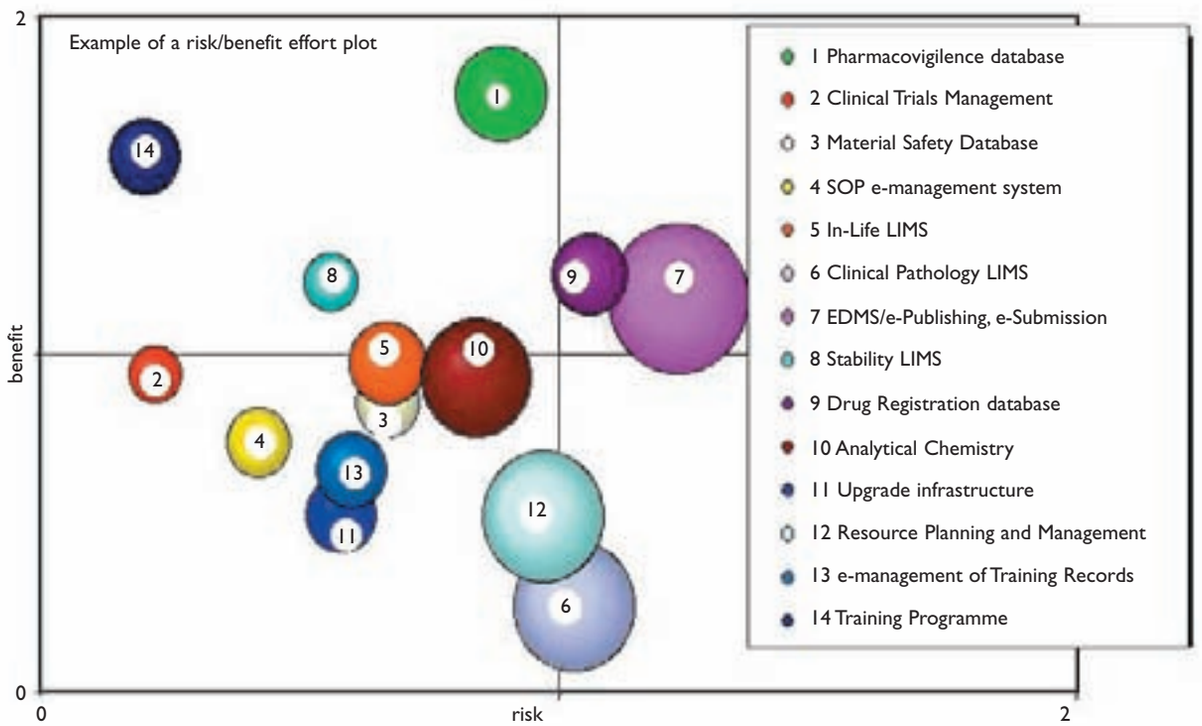


Figure 4

Calculating the expenditure of informatics effort can be a complex task for much more than the cash costs and the informaticians' time needs to be assessed. Commonly, significant user time is required especially in the specification and validation of the project and the quality assurance unit needs to expend considerable energy ensuring the projects are implemented according to the organisation's quality system.

Pseudo three-dimensional plots of these characteristics, especially when used interactively in a management team meeting, can provide useful decision support tools for choosing project priorities (**Figure 4**)[15].

Non-discretionary informatics

Pharmacovigilence

Informatics is increasingly becoming a non-discretionary activity within many pharma business processes ranging right across the value chain – but especially so in the regulatory domains of R&D. Among many regulatory concerns, regulatory authorities are looking to increase their awareness of, and control over, drug safety. They are looking to the pharmaceutical companies to deliver safety information to them electronically[16], coded in MedDRA[17]. Significant business benefits, in addition to these regulatory requirements, will accrue with companies able to support their cross-licensing activities by transferring between themselves pharmacovigilence data sets speedily and accurately.

Dossiers

Furthermore, regulatory authorities are requesting that dossiers be submitted electronically to improve the logistical challenges of handling reams of paper and the ability of assessors to search the dossiers and retrieve information for analysis[18].

Economies of scale

Many regulatory and statutory constraints are being placed upon the industry and its computerised systems eg 21 CFR Part 11 and now HIPAA requirements need to be considered – for big pharma by April 2003 and for SMEs no later than April 2004. The larger pharmaceutical companies have the opportunity to leverage their economies of scale to provide key informatics services in the non-discretionary domains; this is not available to the SMEs.

However, the recent emergence of Application Service Providers (ASPs), to add value to the geographic reach provided by the Internet Service Providers (ISPs), provides the SME with a choice. Rather than build the next generation of R&D informatics applica-

tions in-house, the SME could use an ASP. In principle ASPs could create economies of scale and generate cost efficiencies by creating applications platforms – where necessary 21 CFR Part 11 'open systems' and HIPAA compliant – and shared by many companies.

As Steve Gardner recently wrote: "By strategic outsourcing of elements of the design, implementation and management of their informatics systems, smaller companies can expect to significantly reduce their costs, get access to more experienced staff than they (or in many cases their larger competitors) could recruit, and design and build better systems than they could by themselves."[19]

Furthermore, the increasing availability from ASPs of key R&D informatics applications (eg pharmacovigilence, clinical trials management and data management systems), could provide a real challenge to the pharmaceutical industry corporate IT departments with their skills and reputations based on more conservative models of service provision.

R&D informatics staff

Availability of informaticians

Informatics talent is a scarce commodity. One estimate shows a current shortage of informatics talent in the USA of 300,000. Another suggests that Europe will create another 7.5 million informatics jobs by 2008[20].

To deliver an informatics service is not easy, to find good informaticians, harder. Informaticians need both to understand and keep pace with the developments in the business domains they are supporting and have the ability to track and select appropriate information technologies from this rapidly moving field to provide robust informatics-based business solutions. Furthermore, regulatory constraints continue to become more exacting and need to be understood, interpreted and implemented by the informatician. Other skills are important too; project management and communications being high on the list of skills required by the contemporary informatician[21].

Requirements of informaticians

An example of these demanding requirements of informatics and informaticians was given in a recent paper by Altman where he wrote "the main challenges for biomedical informatics within pharmacogenomics fall into nine areas[22]:

- Representing the diversity of pharmacogenomic data
- Developing standards for data exchange
- Integrating data from multiple data resources
- Mining literature for knowledge
- Using expression data to understand regulation
- Understanding the structural basis for variability
- Using comparative genomics
- Protecting sensitive patient information
- Managing laboratory information"

This illustrates a significant challenge for the SME. To find personnel with such skills is difficult; to attract them to big pharma is a challenge, for an SME it is even harder. The SME is unable to offer the same level of opportunity and funding as the larger companies.

R&D informatics staff training, development and education

Another approach, however, is to take a medium-term view of informatics staffing requirements and to develop informaticians in-house. Identifying potential informaticians is not difficult. Those who are familiar with the business domain, have good communication skills, who display an interest in the requirements for, and an aptitude in use of, information systems are all potential members of the informatics department. It is then the challenge for informatics management to ensure that the informatics department has a high reputation. Its attributes would include customer focus, team working, innovation, hard work and not least fun. Paramount though is a reputation for detailed care and attention to the training, development and education of its members. Suitable candidates will emerge.

It is disappointing that in general the industry finds little opportunity for employees to spend time in different departments. A well-rounded informatician might also have spent time in IT, internal audit, within both scientific and regulatory domains of the R&D business and also in Quality Assurance. What a fascinating career that could be!

The developing market for ASPs may prove to be an increasingly attractive market for the next generation of informaticians who will find specialist companies able to exploit their command of the business domain, technology developments and increasing regulatory burden. Perhaps the SME might look to provide their next generation informatics systems from the ASPs?

User training

"The next big killer application for the Internet is going to be education. Education over the Internet is going to be so big it is going to make e-mail look like a rounding error."[23]

The increasing burden of regulatory requirements generates an increased training load on the users community. Information contained within the guidances for GLP, GCP, GMP[24], 21 CFR Part 11, HIPAA, company quality system and SOPs, all needs to be communicated to the relevant members of the

References

1 SME Small/Medium-sized Enterprises. In the context of this paper the acronym SME is used specifically to denote small/medium sized pharmaceutical companies or biotechnology companies.
2 Pharma 2005 – Silicon Rally, the race to e-R&D – PriceWaterhouseCoopers, 2000.
3 R&D Informatics is the term used to describe all the activities of applying IT to support R&D including eg business analysis, business process change, computational chemistry, cheminformatics, bioinformatics, information science, computer systems validation and information technology.
4 Wise, John. 'Leveraging the Intranet Revolution to Overcome the Challenges of Merger, Market Share, Time to Market and Finding New Leads' – paper given to the IIR Conference 'Information Technology in Research & Development', London, April 1997.
5 Chief Information Officer – the person responsible for informatics within an organisation.
6 Remenyi, Dan et al. 'The effective measurement and management of IT costs and benefits'.
7 Absorption, Distribution, Metabolism, Elimination/ Toxicology.
8 'e-' – a term used to describe web-based informatics.
9 Modified from work by Breckenridge, R, Maester, D, Wise, J, Ziegler, R. 1993.
10 First Consulting Group – www.fcg.com.
11 Farina, Carlo. 'ASP Architecture at NiKem Research, Milan' paper given to INFOTech Pharma 2002, London.
12 Return on Investment.
13 Net Present Value.
14 Internal Rate of Return.
15 Modified from work by Galbraith, J, Wise, J et al. 1999.
16 ICSRs are requested by the regulatory authorities to be transmitted using E2B format.

Continued on page 72

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user (and indeed informatics and IT) community, documented and filed. The geographical dispersal of the user communities in a multi-national SME causes tremendous demands on the travel budget to ensure all personnel are appropriately trained.

Emergence of e-learning platforms provides the SME with the opportunity to minimise travel and lost opportunity costs. Availability of generic courses on the constraints of the regulatory domain will allow cost effective training in the fundamentals of GxPs. Again, a major challenge will be to choose the appropriate partners from the plethora of choices available.

Business development and product cross-licensing[25]

The pharmaceutical industry perceives these activities to be of strategic importance to grow companies and to reinforce their development pipelines. As such they are receiving increased management attention. The critical success factors for such functions will be the ability of the management teams to 'network', the speed with which they can process relevant information to generate the 'leads' and the ability to manage the '-e' documentation packages increasingly associated with the compounds.

Processing relevant information needs to be seen as a discipline within the business development function – not an afterthought. Sophisticated informatics systems that collate news-feeds, integrate in-house information, provide competitor analysis, generate alerts and route them to e-mail, PDAs and mobile phones, enable market analysis, track correspondence need to be designed, resourced and implemented to provide real competitive advantage.

'e'-archive

Managing 'e-' documentation packages will become an increasing challenge. Traditionally the cross-licensing of a product would embrace arrangements to make available necessary parts of the paper documentation package to the relevant parties. However, with the constraints imposed upon the industry by 21 CFR Part 11[26], 'e-documentation' will need to be handled in a rigorous manner within an 'e-archive'. A clearly defined quality system with detailed SOPs would need to be established, the media will need to be managed to accommodate ever-developing technologies, and the 'e-documentation' stored in line with clearly defined records retention policies drawn from the respective guidances[27] and predicate rules.

R&D informatics sociology

"The trouble with people is not that they don't know but that they know so much that ain't so."[28]

Communication

Communication seems such a simple concept. Perhaps this is the reason that management expects it to happen automatically and without effort. However, communication in many organisations, SMEs included, remains sub-optimal and consequently damaging to the business. Impoverished communications can lead to business objectives becoming opaque, priorities being misassigned and roles and responsibilities being confused. To improve communications, conscious effort needs to be expended and robust processes established including convening users' groups.

The user group

For R&D informatics, the simple concept of a 'user group'- ideally chaired by a senior user while the secretariat is managed by informatics – is an effective tool to increase communication between informatics and the user community. In a multi-site organisation, regular meetings of the individual site user group chairmen, again convened and supported by informatics management, can bring a common understanding of the status of the business priorities, the overall resources available to informatics and the performance of the informatics services. Such meetings can encourage rational, consensus-based choice of the R&D informatics portfolio – from the many activities and projects available for consideration.

Conclusion

Let us return to the chart of the R&D informatics value chain with the underlying R&D informatics project portfolio. Superficial examination of the state of the current market for ASP vendors selling into this domain reveals increasing numbers of ASPs addressing this market segment. I have annotated the diagram with just a few examples (**Figure 5**).

The challenge for SME management is to address the following issues:

- Judged by NDA submissions, R&D is no more successful now than 30 years ago – if anything less.
- R&D informatics is underfunded and is underperforming.
- R&D opportunities (and informatics opportunities) are increasing at a rate greater than the resources to exploit them.
- The demands of the regulatory authorities inexorably increase.
- The availability of informaticians is less than R&D requires – and this shortage will continue.
- The SME, compared to big pharma, does not have economies of scale to exploit in building informatics system solutions.

17 MedDRA Medical Dictionary for Drug Regulatory Activities. Supported by MSSO. www.meddramsso.org/
18 Guidance for Industry – Providing Regulatory Submissions in Electronic Format — General Considerations – January 1999 US Department of Health and Human Services, Food and Drug Administration.
19 Gardner, Steve. 'Outsourcing life science informatics solutions'. 2001. Drug Discovery World Volume 2 Issue 3 pp29-36.
20 Ziegler, R. Infotech Pharma 2002, London.
21 Mclucas,Kate. '10 skills: Look past the technology', InfoWorld, Sept 13, 1999.
22 Altman, RB, Klein, TE. Biomedical Informatics. World Market Series Business Briefing, Future Drug Discovery, December 2001.
23 Chambers, John. CEO Cisco Systems (2000).
24 Collectively known as GxP.
25 Business Development – the activity concerned with finding strategic partners to reinforce any component of the value chain. Product cross-licensing – the activity concerned with buying, selling and licensing rights to compounds.
26 21 CFR Part 11 Federal Register/Vol. 62, No. 54/Thursday, March 20, 1997/Rules and Regulations 13465.
27 eg ICH GCP 5.5.11, 21 CFR Part 11.10 a and b.
28 Billings, Josh (aka Wheeler Shaw, Henry), born in Lanesboro, Massachusetts April 12, 1818. A renowned humourist, in his day, Billings was better known and appreciated than his contemporary, Mark Twain.)
29 'The Leopard', Giuseppe Tomasi di Lampedusa.

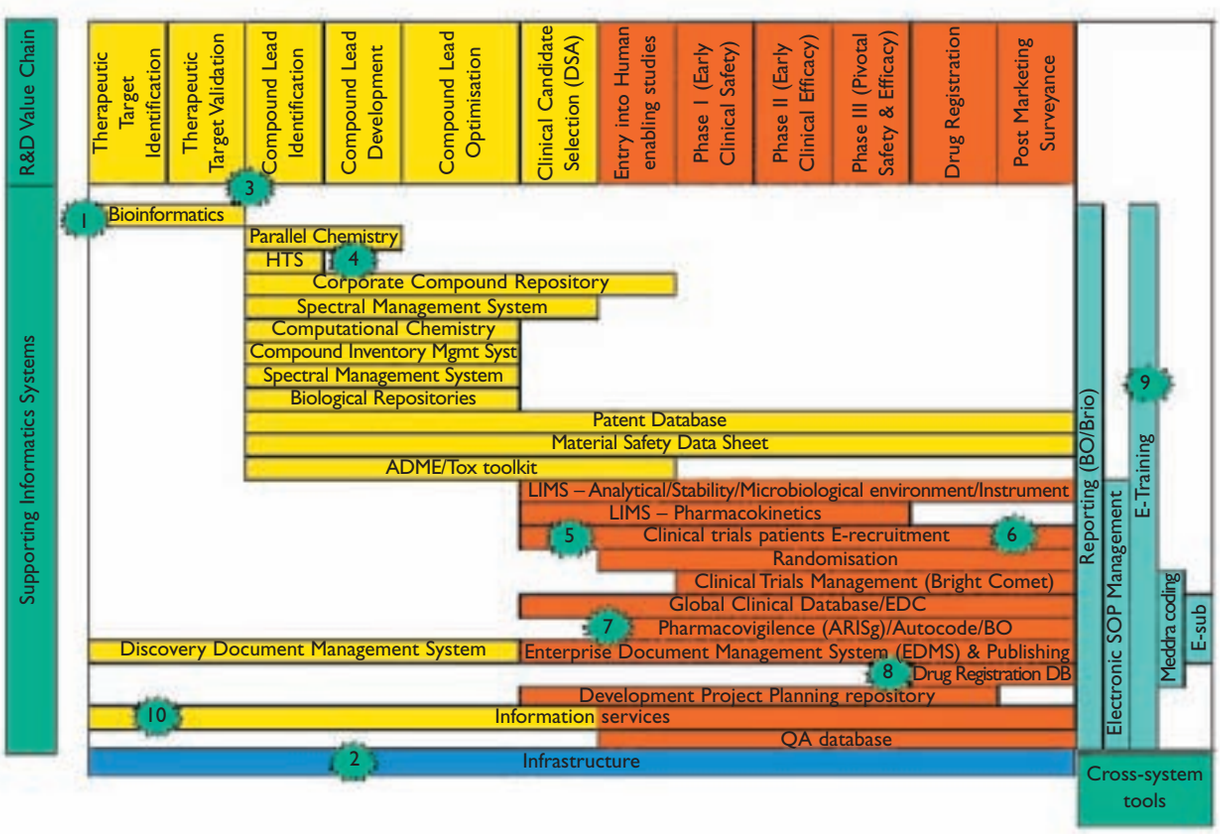
- The SME must have a plan for 'e-'.
- The SME must manage choice from the immense informatics opportunities.
- ASPs exploiting the geographic reach of the ISPs can deliver economies of scale.
- The future of R&D informatics within the SME sector of the global pharmaceutical and biotech industry lies with ASPs.

A Sicilian prince, writing about the political and dynastic upheavals in Italy 150 years ago wrote: "If we want things to stay as they are, things will have to change."[29] …much the same can be said about informatics in SME Research and Development! DDW

John Wise *has been involved with IT for 25 years. Joining the Pharmacology Department of St George's Hospital Medical School, London in the early 1980s he developed interactive neuropharmacological research applications software and was appointed Lecturer in Computing. In the mid-1980s he joined Sandoz Pharma, holding various senior IT positions in the UK and Switzerland and was part of the international team tasked with formulating Sandoz's global IT strategy. In 1995 John became Head of IT for the Imperial Cancer Research Fund before joining Roche as Head of Non-Clinical Development Information Management. He is currently Head of R&D Informatics at Beaufour Ipsen.*

Figure 5

An R&D informatics portfolio



NO	DOMAIN	ACTIVITY	COMPANY NAME	COMPANY URL
1	Discovery	Bioinformatics	Biowisdom	www.biowisdom.com
2	R&D	Infrastructure	Getronics	www.getronics.com
3	Discovery	Bioinformatics/Cheminformatics	Viaken	www.viaken.com
4	Discovery	Cheminformatics	MDLi	www.mdli.com
5	Development	Clinical Trials Mgmt	eResearchTechnology Inc	www.ert.com
6	Development	Clinical Trials	DATATRAK	www.datatraknet.com
7	Development	Adverse Events	Sentrx Inc	www.sentrxinc.com
8	PMS	Registration Tracking	PhaseForward	www.phaseforward.com
9	R&D	Training	EduNeering Inc	www.eduneering.com
10	R&D	Information Services	Rowecom	www.rowecom.com