## TEXT INFORMATION MANAGEMENT SYSTEM (TIMS)

The name "text information management system" is not as widely used as the name "laboratory information management system." Nevertheless, a text documentmanagement systemis essential in preclinical development because huge numbers of text documents and other related information such as images, drawings, and photographs are generated in the area. All these documents and information are considered intellectual property and require protection and easy access.

One of the characteristics of the pharmaceutical industry is large quantities of paperwork, particularly in areas where GMP/GLP are strictly enforced. The slogan "documentation, documentation, and documentation." is always in the mind of laboratory scientists.

The scientists in preclinical development spend quite a large percentage of their working time writing compound documents (reports). The report generation, review, approval, filing, and retrieval process can be very inefficient or even bureaucratic in a pharmaceutical company, partly because of the strict

regulations. The following scenario could be seen often as recently as the late 1980s: The scientist would prepare his report with one type or another of text and graphic software, often through multiple cut-and-paste procedures to include pictures or images. Then the scientist would make hard copies of the report for review by managers and the department head. After all the corrections were made, the scientist would print out another copy for the QA auditor for auditing (this is only done for the documents used for submission). It could take months before the report was finally ready to be filed in the company record center, where photocopies and microfilms were made and indexing took place. When an end user needed a copy of the report, he would have to make a request to the record center for a hard copy.

When TIMS is used in today's workflow, the scientist can use a report template to facilitate report writing. Some cut-and-paste procedures are still needed to include data and figures. After the draft report is completed, the scientist can send the reviewers an electronic link for the document. The reviewers can review the document and make changes and corrections with the "tracking change" function. When the review is completed, the author can choose to accept the changes or deny them. If auditing is needed, the same process can be used. The finalized document is issued within the TIMS by adding an issue date and signatures, if necessary, and converting into an unalterable PDF file. Future changes made after issuance are captured through version control. End users can also access the issued document electronically and remotely. Comparison of the new process vs. the old one has demonstrated the advantages of TIMS.

## Requirements in Preclinical Development

In preclinical development, the GMP/GLP regulations are enforced not only for scientific data but also for text documents. This section discusses several types of controlled text documents used in preclinical development. Most of these documents are managed by the fully validated TIMS. Product specification documents and analytical test methods. In preclinical development, these are important documents and they evolve

along with the development phases. Drug substances and products for clinical trials are tested based on these documents, and so are the stability samples. It is critical to ensure that the analyst will perform the right tests against the right specifications with the correct version of the test method. Therefore a mechanism must be in place to control these documents. This can be done manually or with TIMS. A manually controlled system would require the analyst to sign out hard copies of the documents from a central location. After the testing is done, the analyst would have to return these controlled documents to the central location. Sometimes mistakes can be made with regard to the correct documents, and this will result in repetition and unnecessary investigation. If TIMS is implemented, the analyst can obtain the documents from the secured database and then the documents should be destroyed after the test is completed.

***Standard operating procedures (SOPs)*** - The SOPs are controlled in a way similar to that of specification documents and analytical methods. It must be ensured that the correct versions of the SOPs are accessed and used by the scientists. After use, the hard copies should be destroyed and disposed of properly. An added requirement is that the SOPs should be accessible during working hours without interruption. Hard copies should be available at a manageable location so that the SOPs are available when the electronic system is down.

***Research reports*** - Research reports such as stability reports, method validation and transfer reports, and pharmaceutical development reports are key documents used for NDA/MAA filings. These documents are strictly version controlled.

***Laboratory notebooks*** - It may be debatable to consider laboratory notebooks as text documents, but they should be mentioned here because of their importance in preclinical development. Laboratory notebooks are used to record experimental procedures, observations, raw data, and other important information. Although laboratory notebooks are rarely used for submission to regulatory agencies directly, are available for inspection by the authorities in the Preapproval

But still most of the pharmaceutical companies using paper based laboratory notebooks.

## CURRENT TIMS PRODUCTS

Various so-called Enterprise Content Management (ECM) systems are commercially available that can meet different end user requirements. TIMS used in preclinical text document management usually is a simplified version of ECM. At the highest enterprise platform level, ECM vendors include Documentum, File Net, Interwoven, Stellent, and Vignette. At a lower level, the upper-tier products are provided by Day Software, Fat Wire, and IBM. For less costly products, there are Ingeniux, Paper Thin, Red Dot Solutions, and Serena Software. It should also be pointed out that the cost of acquiring and maintaining a fully validated TIMS is much higher than that of a non-GMP/GLP system. Therefore many of the non-GMP/GLP documents in early-phase development are managed with nonvalidated TIMS.

## CDS (CHROMATOGRAPHIC DATA SYSTEM)

The importance of CDS is directly related to the roles that chromatography, particularly high-performance liquid chromatography (HPLC) and gas chromatography (GC), play in pharmaceutical analysis. HPLC and GC are the main workhorses in pharmaceutical analysis. In today's pharmaceutical companies, development work cannot be done without HPLC and GC. CDS are also used for several other instrumental analysis technologies such as ion (exchange) chromatography (IC), capillary electrophoresis (CE), and supercritical fluid chromatography (SFC).

### History of CDS

In the 1960s and early 1970s, chromatographs were relatively primitive and inefficient. Chromatographers had to use microsyringes for sample injection and stopwatches for measurement of retention times. The chromatograms were collected with a strip chart recorder. Data analysis was also performed manually. Peak areas were obtained by drawing a "best fit" triangle manually for each peak and then using the

equation Area = ½ Base × Height. At that time, the management of chromatographic data was essentially paper based and very inefficient.

However, compared with the traditional analytical methods, the adoption of chromatographic methods represented a significant improvement in pharmaceutical analysis. This was because chromatographic methods had the advantages of method specificity, the ability to separate and detect low-level impurities. Specificity is especially important for methods intended for earlyphase drug development when the chemical and physical properties of the active pharmaceutical ingredient (API) are not fully understood and the synthetic processes are not fully developed. Therefore the assurance of safety in clinical trials of an API relies heavily on the ability of analytical methods to detect and quantitate unknown impurities that may pose safety concerns.

This task was not easily performed or simply could not be carried out by classic wet chemistry methods. Therefore, slowly, HPLC and GC established their places as the mainstream analytical methods in pharmaceutical analysis.

As chromatographic methods became more and more important in the pharmaceutical industry as well as in other industries, practical needs prompted instrument vendors to come up with more efficient ways for collecting and processing chromatographic data. In the mid-1970s, the integrator was introduced. At first, the integrator worked similarly to a strip chart recorder with the added capabilities of automatically calculating peak area and peak height. Because of limited available memory, chromatograms could not be stored for batch processing. However, new models with increasing capabilities quickly replaced the older ones. The newer models had a battery back-up to maintain integration parameters and larger memory modules to allow the storage of chromatograms for playback and reintegration. At that time, the integrator increased productivity and efficiency in pharmaceutical analysis, which in turn made HPLC and GC even more popular.

For some instrument vendors, the early CDS were developed as proprietary products to help with the sale of instruments. The first generation of CDS systems were based on a working model of multiuser, time-sharing minicomputers. The minicomputers were connected to terminals in the laboratory that the analysts would use. The detector channels of the chromatographs were connected to the data system through a device called the analog-to-digital (A/D) converter, which would convert the analog signals from the detectors into digital signals. In the late 1970s, Hewlett-Packard introduced the HP-3300 series data-acquisition system. Through the A/D converters, the HP system was able to collect chromatographic data from up to 60 detector channels.

This represented the beginning of computerized chromatographic data analysis and management. Because the CDS used a dedicated hardware and wiring system, it was relatively expensive to install. It was also difficult to scale up because more minicomputers would be needed with increases in the number of users.

Another drawback of the system was that the performance of the system would degrade as the number of users increased. The next generation of CDS systems did not appear until the start of the personal computer (PC) revolution in the 1980s. The early PCs commercialized by Apple and IBM were not very reliable or powerful compared with today's PCs. The operating systems were text based and difficult to use.

However, it was economically feasible to put them on the desktop in each laboratory, and they were evolving rapidly to become more powerful in terms of hardware and software. By the early 1990s, the PCs were reaching the calculation speed of a minicomputer with a fraction of the cost. A graphicsbased operating system also made them more user-friendly. Taking advantage of the PC revolution, a new generation of CDS appeared on the market that utilized a client/server model. In the new CDS, the client provided the graphical and user interface through a PC and was responsible for some or most of the application processing. The server typically maintained the

database and processed requests from the clients to extract data from or update the database. This model was adopted widely in the industry for almost a decade because of its scalability. It also facilitated the activities of data sharing, method transfer, result review and approval, and troubleshooting at different laboratories and locations. It also overcame the problem of scale-up. During this period of time, in parallel with the progress in CDS, chromatography itself was developing rapidly. Instrumentation had adopted modular design so that each functional part became more reliable and serviceable.

Progress in microelectronics and machinery made the solvent delivery pump more accurate and reproducible. The accuracy and precision of auto samplers also were significantly improved. Compared with the time when chart recorders or integrators were used, the fully automated HPLC could now be programmed to run for days and nights nonstop. Results could also be accessed and processed remotely. With the help of sophisticated CDS, chromatography finally established its dominance in pharmaceutical analysis.

As instrumental analysis played an increasingly important part in pharmaceutical development, an ever-larger percentage of the data in Good Manufacturing Practice and/or Good Laboratory Practice (GMP/GLP) studies were captured and stored electronically. As CDS became more sophisticated, new functions such as electronic approval became available. However, the legal issues related to electronic signatures needed to be addressed and recognized by the regulatory authorities. To clarify the confusion and provide clear guidelines regarding electronic data, the FDA issued 21 CFR Part 11 rules to address concerns regarding the electronic media of scientific data.

With respect to the FDA's expectations, the CDS operated with the client/server model had a significant drawback. In the client/server model, the client must retain parts of the applications. To fulfill the requirements of system qualification, performance verification, and validation, one must validate not only the server, but also each PC used by the client. This created an enormous burden for the customer, which resulted in the adoption of a new operating model of server-based computing.

# LABORATORY INFORMATION SYSTEM (LIMS)

A **laboratory information management system** (LIMS), sometimes referred to as a **laboratory information system** (LIS) or **laboratory management system** (LMS), is a software-based laboratory and information management system with features that support a modern laboratory's operations. Key features include — but are not limited to — workflow and data tracking support, flexible architecture, and data exchange interfaces, which fully "support its use in regulated environments". The features and uses of a LIMS have evolved over the years from simple sample tracking to an enterprise resource planning tool that manages multiple aspects of laboratory informatics.

# DIFFERENT TYPES OF LIMS

The implementation of LIMS requires a significant amount of investment in capital money and manpower. There are large numbers of established vendors that provide commercial LIMS with a similar range of core functionality, but few of them are dedicated to the pharmaceutical industry because of the market size (Table). The following discussion is not intended to categorize different types of LIMS; rather, we briefly point out the most obvious characteristics of different LIMS. LIMS may possess certain distinctive features, but their core functionalities may be very similar.

### *Customer-tailored LIMS*

In an implementation of this type of LIMS, the customer purchases a generic product from the vendor. The vendor and customer will work together over a period of time to configure the software to adapt it to meet end user needs. This usually involves extensive programming, which can be performed by the trained end user or dedicated supporting personnel on the customer side. Programming support is usually needed for the entire life of the LIMS to accommodate changes in development projects.

The advantage is that the LIMS functions relatively closely to the business practices of the customer and the system can be tailored to fit the needs of the customer's development projects. The disadvantage is that it takes considerable resources to implement and maintain the LIMS.

### *Preconfigured LIMS*

This LIMS does not require extensive customer programming. To meet specific needs of end users, the vendors provide a comprehensive suite of configuration tools. These tools allow end users to add new screens, menus, functions, and reports in a rapid and intuitive manner. The tools also allow the LIMS to be more easily integrated with other business applications such as document processing, spreadsheets, and manufacturing systems.

## SPECIALIZED LIMS

This type of LIMS is based on the fact that certain laboratories have a range of well-defined processes (e.g., stability testing) that are performed according to a specific set of regulations and by using well-established tests. The tests are done according to industry-wide accepted protocols. Specialized LIMS are tailor-made for certain types of laboratories. Therefore the performance can be optimized for clearly defined work process.

**Table. Selected LIMS Vendors Specialized in Pharmaceutical Industry**

| Product | Vendor | URL |
|---|---|---|
| Debra | LabLogic Systems Ltd | www.lablogic.com |
| Q-DIS/QM | Waters | www.waters.com |
| QC Client | Agilent | www.agilent.com |
| WinLIMS | QSI | www.lims-software.com |
| ACD/SLIMS | Advanced Chemistry Development | www.acdlabs.com |
| V-LIMS | Advance Technology Corp | www.vetstar.com |
| VET/HEX | HEX Laboratory Systems | www.hexlab.com |
| BioLIMS | PE Informatics | www.pebiosystems.com |
| LabCat | Innovative Programming Assoc. | www.labcat.com |

### *LIMS as rented service*

The application service provision provider (ASP) is a means of obtaining access to software applications without the need to acquire expensive licenses and hardware or employ high-cost support resources. The application is hosted on a third-party site with system maintenance, backup, and recovery provided by a third party. Products and services can be rented for a contract period on a fixed cost per user/per month basis. The advantages of obtaining LIMS in this fashion include reduced cost in initial investment and reduced requirement of resources for maintaining the LIMS. The continued security and integrity of the data transferred over the Internet is a major concern for this type of LIMS.

## CURRENT TIMS PRODUCTS

Various so-called Enterprise Content Management (ECM) systems are commercially available that can meet different end

**BIOINFORMATICS**

## Benefits of Bioinformatics

CADD methods and Bioinformatics tools offer significant benefits for drug discovery programs which are discussed briefly below:

### *Costs*

The Tufts Report suggests that the cost of drug discovery and development has reached $800 million for each drug successfully brought to market. Many biopharmaceutical companies now use computational methods and Bioinformatics tools to reduce this cost burden. Virtual screening, lead optimization and predictions of bioavailability and bioactivity can help guide experimental research. Only the most promising experimental lines of inquiry can be followed and experimental dead-ends can be avoided early. Growth of the Bioinformatics market is primarily attributed to its increased usage in the pharmaceutical industry. The application of Bioinformatics in drug discovery and development is expected to reduce the annual cost of developing a new drug by 33 percent, and the time taken for drug discovery by 30 percent. That is a valuable proposition in the global drug discovery market expected to be worth $25.1

billion in 2006. The global Bioinformatics market is forecast to grow to $3 billion in 2010 from its current $1.4 billion, for a compound annual growth rate (CAGR) of 15.8 percent, says BCC Research. Analysis software and services should drive this growth, rising to $1.2 billion in 2010 from $450 million in 2005.

### *Time-line*

The predictive power of CADD can help drug research programs choose only the most promising drug candidates. By focusing drug research on specific lead candidates and avoiding potential "dead-end" compounds, biopharmaceutical companies can get drugs to market more quickly.

### *Insight*

One of the non-quantifiable benefits of CADD and the use of Bioinformatics tools is the deep insight that researchers acquire about drug-receptor interactions. Molecular models of drug compounds can reveal intricate, atomic scale binding properties that are difficult to envision in any other way. When we show researchers new molecular models of their putative drug compounds, their protein targets and how the two bind together, they often come up with new ideas on how to modify the drug compounds for improved fit. This is an intangible benefit that can help design research programs.

CADD and Bioinformatics together are a powerful combination in drug research and development. An important challenge for us going forward is finding skilled, experienced people to manage all the Bioinformatics tools available to us, which will be a topic for a future article.

Bioinformatics thus clearly allows exploitation of the data that is available and this together with increased understanding of molecular biology and the molecular basis of disease greatly improves the drug discovery process. The data from the Human Genome Project has availed great opportunities for drug discovery and streamlining the choice of targets to support the drug discovery pipeline. The methods outlined above which are used in computer aided drug design mean that finding an

attractive target is not an issue. The only concern is validating those targets to come up with the ones likely to succeed and here Bioinformatics tools are 'the saviour'

Bioinformatics tools can be used to gather all the necessary information about potential targets. This information includes nucleotide and protein sequencing, homologue mapping, function prediction, pathway information, disease associations, variants, structural information, gene and protein expression data and species distribution among others. The accumulation of this information into databases about potential targets means pharmaceutical companies can save themselves much time, effort and expense exerting bench efforts on targets that will ultimately fail.

As compared to the traditional method of drug discovery where a compound with potential pharmacological activity is isolated and then tested on animals and subsequently in people during clinical trials, using Bioinformatics tools it is now easy to start with the compound which specifically targets proteins. Thus the whole process is no longer on a trial and error basis like the traditional approach. This is the way to go for pharmaceutical companies.

Now armed with the resources from information technology and the human genome data, it only makes good economic sense to invest in the Bioinformatics sector and help make it work to their advantage. No more do scientists have to work hard coming up with a lead only for it to fail when finally tested in humans, resulting in incurring losses. Using Bioinformatics is more like a marketing aspect where one assesses the needs of the consumer and then comes with a product to meet those needs, instead of making a product first and then imposes it onto the consumer hoping that it will meet their needs. Surely the first method is the winner and Bioinformatics presents such a unique opportunity.

Although Bioinformatics is considered to have generated a lot of excitement and yet failed to deliver what it promised, that does not remove the clear advantages Bioinformatics brings to drug discovery. Bioinformatics may be considered to be a discipline in its infancy and as such it needs time to grow and really get organized. It is important to note that at the and of it, it

is the patient buying prescription drugs from a chemist who has to enjoy the benefit of medicine which works and has minimal side effects at most importantly at an affordable price. The pharmaceutical industry should never lose this focus as it is easy to only consider productivity and profitability at the expense of the patient.

It is exciting to think of the possibilities that Bioinformatics may bring forth in terms of finding drugs for conditions such as cancer, AIDS, tuberculosis. The benefit for the industry is obviously in cutting costs and speeding up the process to get new drugs onto the market. For the common man on the street the major benefits would be of course drug affordability as well as access to life saving drugs in a shorter time. Many lives have been lost due to unavailability of such drugs and embracing Bioinformatics may reduce the loss and greatly improve the lives of humanity.

## Conclusion

Bioinformatics clearly may be the answer to solve the drug discovery and cost woes of the pharmaceutical industry. Though still in its infancy and having been considered by some as having up to now failed to deliver and live up to its theoretical potential, the advantages and unique opportunities it brings can not be ignored. It holds one of the keys to dramatically cut the costs involved in drug discovery and ultimately the price of the drugs to the patients at the end of the chain. By eliminating potential drug failures early on during the process, it also helps cut the time scientists take to get a drug from the laboratory to the chemist's shop as they only concentrate their efforts on the leads which hold the greatest potential only. Thus if properly utilized, the pharmaceutical industry will increase the number of drugs in their pipelines which has been dwindling, drugs which are more effective due to the Bioinformatics tools employed. Reduced time of drug discovery also benefits the patients immensely as they will have quicker access to life saving drugs at an affordable price.

Thus Bioinformatics has the potential to hugely decrease the risk, cost and expertise required for the early stages of drug

perception of the pharmaceutical industry due to the ever spiraling drug prices, recalls and recent warnings about popular prescription medications. In an attempt to improve and reduce the cost of drug discovery, the pharmaceutical industry has recently turned to Bioinformatics. Some analysts predict that Bioinformatics could help cut in half the cost of creating a drug and shave two to three years off its development

## History and Definition of Bioinformatics

Bioinformatics started over a century ago when Gregor Mendel, an Austrian monk cross-fertilized different colors of the same species of flowers. Mendel illustrated that the inheritance of traits could be more easily explained if it was controlled by factors passed down from generation to generation. Since Mendel, Bioinformatics and genetic record keeping have come a long way.

In 1988, the Human Genome organization (HUGO) was founded. The first complete genome map was published of bacteria **Haemophilus Influenza**. In 1990, the Human Genome Project was started. By 1991, a total of 1879 human genes had been mapped. In France, in 1993, Genethon, a human genome research center produced a physical map of the human genome. Three years later, Genethon published the final version of the human genetic map. This concluded the end of the first phase of the Human Genome Project.

Bioinformatics was fuelled by the need to create huge databases, such as Genbank, EMBL and DNA Database of Japan to store and compare the DNA sequence data erupting from the human genome and other genome sequencing projects. It enables researchers to analyze the terabytes of data being produced by the Human Genome Project. Gene sequence databases and related analysis tools all help scientists to determine whether and how a particular molecule is directly involved in a disease process. That in turn, helps them find new and better drug targets. Bioinformatics can be thought of as a central hub that unites several disciplines and methodologies as shown below. It brings together several activities and this may explain why we get so many definitions for Bioinformatics. The

diagram below graphically represents the several methodologies which together make up the discipline of Bioinformatics.

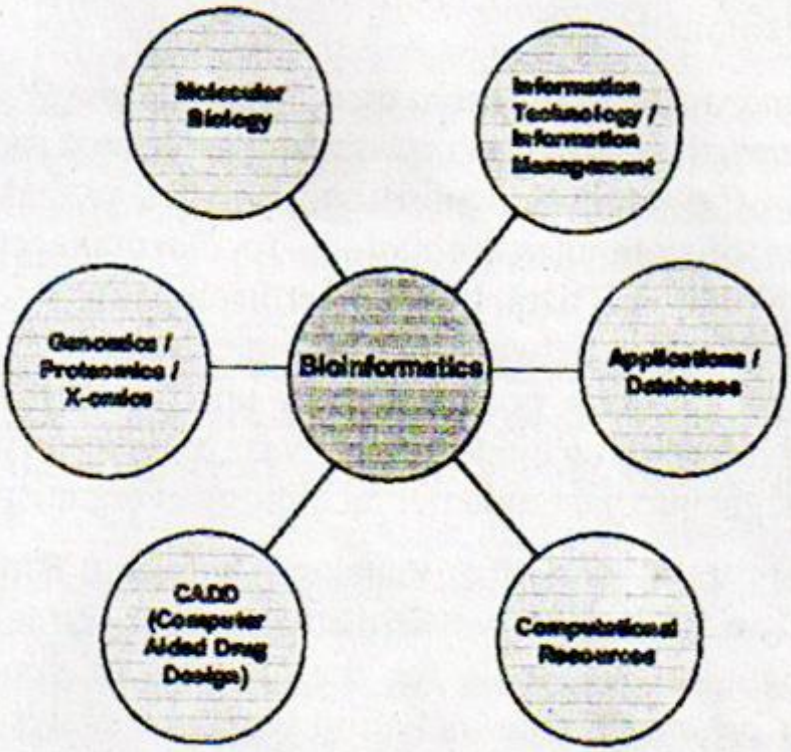


**Fig. Several methodologies which together make up the discipline of Bioinformatics**

Computer-Aided Drug Design (CADD) is a specialized discipline that uses computational methods to simulate drug-receptor interactions. CADD methods are heavily dependent on Bioinformatics tools, applications and databases. As such, there is considerable overlap in CADD research and Bioinformatics.

Bioinformatics uses computers to store, organize, generate, retrieve, analyze and share sequences, structures, functions, pathways and genetic interactions. The definition of Bioinformatics is not universally agreed upon. Generally speaking, it is defined as the creation and development of advanced information and computational technologies for problems in biology, most commonly molecular biology (but increasingly in other areas of biology). As such, it deals with methods for storing, retrieving and analyzing biological data, such as nucleic acid (DNA / RNA) and protein genomic, biological and chemical data to support the drug discovery process.

Some people construe Bioinformatics more narrowly, and include only those issues dealing with the management of

application of computers to the collection, organization, analysis, manipulation, presentation, and sharing of biologic data to solve biological problems on the molecular level. According to Frank Tekaia, bioinformatics is the mathematical, statistical and computing methods that aim to solve biological problems using DNA and amino acid sequences and related information.

The term bioinformatics was coined by Paulien Hogeweg in 1979 for the study of informatic processes in biotic systems. The National Center for Biotechnology Information (NCBI, 2001) defines bioinformatics as: "Bioinformatics is the field of science in which biology, computer science, and information technology merge into a single discipline. There are three important sub-disciplines within bioinformatics: the development of new algorithms and statistics with which to assess relationships among members of large data sets; the analysis and interpretation of various types of data including nucleotide and amino acid sequences, protein domains, and protein structures; and the development and implementation of tools that enable efficient access and management of different types of information."

Bioinformatics is a scientific discipline that has emerged in response to accelerating demand for a flexible and intelligent means of storing, managing and querying large and complex biological data sets. The ultimate aim of bioinformatics is to enable the discovery of new biological insights as well as to create a global perspective from which unifying principles in biology can be discerned. Over the past few decades rapid developments in genomic and other molecular research technologies and developments in information technologies have combined to produce a tremendous amount of information related to molecular biology. At the beginning of the genomic revolution, the main concern of bioinformatics was the creation and maintenance of a database to store biological information such as nucleotide and amino acid sequences.

# HOSPITAL INFOMATION SYSTEM (HIS)

A **hospital information system** (**HIS**) is an element of health informatics that focuses mainly on the administrational needs of hospitals. In many implementations, a HIS is a comprehensive, integrated information system designed to manage all the aspects of a hospital's operation, such as medical, administrative, financial, and legal issues and the corresponding processing of services.

Hospital Information System architecture has three main levels, Central Government Level, Territory Level, and Patient Carrying Level. Generally, all types of hospital information system (HIS) are supported in client-server architectures for networking and processing. Most work positions for HIS are currently resident types. Mobile computing began with wheeled PC stands. Now tablet computers and Smartphone applications are used.

Goal of Hospital Information System (HIS) is supporting hospital activities in the levels of practical, Tactical, and strategic. In other words, goal of hospital information system (HIS) is using of computers and communications equipment for collecting, storing, processing, readout, and communication between patients cares with administrative data on all hospital activities and comply needs of all consumers system .In academic hospitals, also research and training support is one of the hospital information system (HIS) goals. Generally the main goals hospital information system (HIS) can be summarized in the following:

- Improving staff efficiency
- To remove duplication and unnecessary procedures
- Using computers as work tools
- Statistics and data mining techniques faster and more accurate
- Improving quality of health care status of
- To create a modern working methods and systems and standardized hospital
- Data communication systems, medical engineering
- Data communication between hospitals and medical centers in
- The country reaching a distributed database in the country and make its relationship with the World Health Networks
- Promote community health

## A. History of Hospital Information System (HIS)

Reports relating to the use of computers returns to support clinical data management activities in 1950, Although most early systems were created to provide financial and repayment goals, but they was the founder of modern electronic records. Until 1960, hospital information system (HIS) emerged and probably the first hospital information system, data systems was Technician that was created in the system of nursing stations. The first time it was created in a hospital Kamynv, Mountain in December 1971 (EI Camino, Mountain.

Many countries including European countries have moved toward automation hospital information system since the early 1980 .This system developed significantly until now, and it has been an integrated system and with the inner core that called electronic medical records (EMR) from one inconsistent system. Using hospital information system (HIS)was introduced in Iran in 1378 and was launched in the hospital anymore, Mashhad, Yazd, and Zanjan be as a pilot project for the first time. Thus, in 1380 the country's first e-hospital, carried out in the 313-bed hospital Imam Hussein of Shahrood, to the national pilot with the cost of 800 million Rials .One of the positive results of the implementation of electronic information system was 12 percent reduction of medication in this hospital.

## B. The Importance and Necessity of Establishing Hospital Information System (HIS)

Due to extensive changes in medical technology and increased expectations of patients, in the twenty-first century hospitals that lacks hospital information system (HIS), they have nothing to say and will not have the ability to compete with other hospitals.

The most important necessity and reasons for hospital information system automation are Inefficiency manual procedures, the growth of medical research in the world, insurance industrial development and changing reimbursement techniques to the centers of contracts, new methods of medical education, medical facilities great achievement, and increasing professional in Employees and development how hospital

catering and management, growing health costs, increased patient expectations, the associated need for medical centers and medical professionals together and etc. Also a good management information system is necessary to evaluate the quality of care for patients. So the reasons for using these systems can be summarized as follows:

- Generation of alert and Reminds: HIS systems help with the creation of Wake series warning messages to remind doctor in diagnosis. For example, patient has an abdominal pain that is may be 45 diseases that have the same symptoms but doctor remembers only 10 of them.
- Critical Pathway of Decisions: HIS systems help a doctor in serious cases. In very serious cases, that there isn't the opportunity for doctor to decide, these systems help the doctor and bring his response quickly in emergency cases.
- Automatic reporting: one of advantages and performances of HIS systems is that can be provided report of patient's diagnostic - care information automatically by them.
- Reduce cost: HIS systems effect very significant in reducing the costs. So if you have detection algorithms in the system, you won't need to review Problem Oriented of patient. In this case you won't require performing additional tests and etc.
- Access to diagnostic information – care of patient with a PC: using of the appropriate Work station, physician can access patients and hospitals easily from your location or where he/she is present.
- Suitable Administration: One of the benefits of HIS systems is that allow the patient to call the hospital network from home and reserve time to meet with the doctor. Thus make an Appointment is much easier.
- Reducing errors: because all data have been collected in one place, fewer mistakes occur.

## CHARACTERISTICS OF HIS

Properties and characteristics of hospital information system (HIS) as follows:

- It acts based on standard.
- It doesn't make any mandatory in existing manual system, but it matches itself with these systems.
- It acts based on "medical events" and is independent of the cycle of moving patients.
- Using this system, the previous manual and the current trend does not change much .
- It keeps the old computer systems and promotes and improves their futures.
- It offers the best solution for coordination between different lines of work and different units in the hospital
- It coordinates all wards and hospital system.
- It increases the quality of decision making and managerial.
- It includes rich knowledge-based medicine databases such as SNOMED and ICD-10.
- The data entry are required to type in only 2 %of cases and in 98 %cases, for data entry, clicking method is used by the help of the mouse.
- Operation is very simple and completely visual and user-friendly.
- Smart cards are used for identification and control of hospital staff access to patient records (to enhance security).
- It is equipped with video conferencing system between health care professionals.
- It is equipped with knowledge-based intelligent system for diagnosis and treatment.
- It provides Access to information via the Internet to communicate with the mobile phone.
- Filing and retrieval of medical information dense is possible to easy access to the complex and stratified set of data.
- It is equipped with open standards for the implementation of local language.
- It allows to people's common use of medical information recorded and Protocol Guide electronically.
- Using multimedia technology, audio and video recording various Information is possible in it.

## USE OF INTERNET IN PHARMACY

Internet is collection of huge data. And this data is available for us in just a one click. Internet is useful tool in literature survey. Books are also available on the internet. Various research journals can be easily accessed via internet. There are number of web-sites which are related to pharmacy field. Some of these web sites are as follows;

1. **www.phrma.org** Organization representing America's pharmaceutical research companies provides details of drug development, industry news, and health guides.
2. **www.healthcareforums.com** Created to facilitate interaction among healthcare professionals on specific topics which includes discussion of cases, research and other relevant issues.
3. **www.astra.com** This is official web-site of ASTRA pharmaceuticals which produces medications for respiratory tract, cardiovascular and gastrointestinal diseases, and for pain relief. Includes press releases.
4. **www.biogen.com** Company principally engaged in developing genetically-engineered human pharmaceuticals. With career advice, and drug information.
5. **www.gene.com** Develops pharmaceuticals mostly for the treatment of genetic disorders. Includes a listing of the major drugs and their uses.
6. **www.genzyme.com** Company that specializes in biotechnology and health care products. With career, product, and services information.
7. **www.pfizer.com/main.html** Find out about research projects and career opportunities at this Pfizer pharmaceuticals. Includes health education and pharmaceutical advice section.
8. **www.roche.com** Roche produces pharmaceuticals and products for treatment of HIV, obesity and cardiac conditions. Offers news and company information.

9. **www.pharmweb.net/pwmirror/pwk/pharmwebk.html** Listing of international pharmaceutical regulatory bodies including the US Food and Drug Administration.

10. **http://www.druginfonet.com** Drug information, disease information, Ask the Expert, Pharmaceutical Manufacturer Information, Healthcare news and information, Medical References / libraries.

11. **http://www.fda.gov/default.htm** Useful for checking adverse reaction reports for dietary supplements and drug interactions. The Orange book approved drug products is also available on-line here, as well as orphan drug products (with links to other web-sites for rare disease/orphan product information). Contains an alphabetical listing of drugs licensed in the US and the corresponding package inserts. Lists the latest information on drug recalls, drug shortages, and changes in labeling

12. **www.ijpc.com** Alphabetical Index of formulations found in the International Journal of Pharmaceutical Compounding. Specialty articles on compounding

13. **http://www.pharmainfo.com** Pharmaceutical News, Pharmaceutical Articles, and Pharmaceutical blogs

14. **www.fda.gov/cvm/** Searchable listing provides facts and figures on all animal drug products approved by the FDA.

15. **www.aaps.org** Information on officers, activities and membership from the American Association of Pharmaceutical Scientists

16. **http://www.sciencedirect.com** Contains research and review articles related to pharmacy field

## COMPUTER ADDED DRUG DESIGN

Drug design, also sometimes referred to as rational drug design, is the inventive process of finding new medications based on the knowledge of the biological target. This type of drug design can be assisted by computer softwares. Software will generate number of lead molecules depending upon the feed data and among these; compound of interest can be developed and tested. If such process is carried out manually then it will be time consuming and tedious. But use of computer reduces time hugely.

Molecular modeling and molecular graphics have shown dramatic growth and are becoming integral part of drug discovery process. Molecular modeling is the generation, manipulation and representation of three dimensional form of molecule. Molecular graphics refers to the use of computer graphics to represent the molecular structure. In the past synthetic chemists have used molecular models, but computer modeling has enhanced the detailed display of molecular structures.

Various types of softwares are available, like Auto Dock (The Scripps Research Institute), Combi BUILD (Sandia National Labs), Dock Vision (University of Alberta), HINT! (Virginia Commonwealth University), LIGPLOT (University College of London), SITUS (Scripps Research Institute), DOCK (UCSF Molecular Design Institute), Sanjeevani (Indian Institute of Technology, New Delhi), Bio-Suite (Tata Consultancy Services Ltd.), Maestro, Macro Model 5.5, Delphi.

Some popular drugs are discovered by using computer assisted drug design.(Table.)

Table. Marketed Pharmaceuticals whose discovery was assisted by computers

| Generic name | Brand name | Year approved in United States | Discovery assisted by | Activity |
|---|---|---|---|---|
| Norfloxacin | Noroxin | 1983 | QSAR | Antibacterial |
| Losartan | Cozzar | 1994 | CADD | Anti-hyeprtensive |
| Dorzolamide | Truspot | 1995 | CADD/ SBDD | Antiglaucoma |
| Ritonavir | Norvir | 1996 | CADD | Antiviral |
| Indinavir | Crixivan | 1996 | CADD | Antivairal |
| Donepezil | Aricept | 1997 | QSAR | Anti-Alzheimer's |
| Zolmitriptan | Zomig | 1997 | CADD | Animigraine |
| Nelfinavir | Viracept | 1997 | SBDD | Antiviral |
| Amprenavir | Agenerase | 1999 | SBDD | Antivtral |
| Zanamavir | Relenza | 1999 | SBDD | Antiviral |
| Oseltamavir | Tamiflu | 1999 | SBDD | Antiviral |
| Lopinavir | Aluviran | 2000 | SBDD | Antiviral |
| Imatinib | Gleevec | 2001 | SBDD | Antineoplastic |
| Erlotinib | Tarceva | 2004 | SBDD | Anineoplastic |
| Ximelagatran | Exanta | 2004 | SBDD | Anticoagulant |

QSAR: Quantitative structure-activity relationship, CADD : Computer Assisted Drug Design, SBDD : Structure Based Drug Design

## PATIENT INFORMATION SYSTEM

In medicine, monitoring is the observation of a disease, condition or one or several medical parameters over time. Display device of a medical monitor as used in anesthesia

It can be performed by continuously measuring certain parameters by using a medical monitor (for example, by continuously measuring vital signs by a bedside monitor), and/or by repeatedly performing medical tests (such as blood glucose monitoring with a glucose meter in people with diabetes mellitus).

Transmitting data from a monitor to a distant monitoring station is known as telemetry or biotelemetry.

## Contents



## Classification by target parameter

Monitoring can be classified by the target of interest, including:

1. **Cardiac monitoring,** which generally refers to continuous electrocardiography with assessment of the patient's condition relative to their cardiac rhythm. A small monitor worn by an ambulatory patient for this purpose is known as a Holter monitor. Cardiac monitoring can also involve cardiac output monitoring via an invasive Swan-Ganz catheter.
2. **Hemodynamic monitoring,** which monitors the blood pressure and blood flow within the circulatory system. Blood pressure can be measured either invasively through an inserted blood pressure transducer assembly, or noninvasively with an inflatable blood pressure cuff.
3. **Respiratory monitoring,** such as:

Pulse oximetry which involves measurement of the saturated percentage of oxygen in the blood, referred to as SpO2, and measured by an infrared finger cuff.

Capnography, which involves $CO_2$ measurements, referred to as EtCO2 or end-tidal carbon dioxide concentration. The respiratory rate monitored as such is called AWRR or airway respiratory rate).

Respiratory rate monitoring through a thoracic transducer belt, an ECG channel or via capnography

1. Neurological monitoring, such as of intracranial pressure. Also, there are special patient monitors which incorporate the monitoring of brain waves (electroencephalography), gas anesthetic concentrations, bispectral index (BIS), etc. They are usually incorporated into anesthesia machines. In neurosurgery intensive care units, brain EEG monitors have a larger multichannel capability and can monitor other physiological events, as well.
2. Blood glucose monitoring
3. Childbirth monitoring
4. Body temperature monitoring through an adhesive pad containing a thermoelectric transducer.

## Vital parameters

An anesthetic machine with integrated systems for monitoring of several vital parameters, including blood pressure and heart rate.

Monitoring of vital parameters can include several of the ones mentioned above, and most commonly include at least blood pressure and heart rate, and preferably also pulse oximetry and respiratory rate. Multimodal monitors that simultaneously measure and display the relevant vital parameters are commonly integrated into the bedside monitors in critical care units, and the anesthetic machines in operating rooms. These allow for continuous monitoring of a patient, with medical staff being continuously informed of the changes in general condition of a patient. Some monitors can even warn of pending fatal cardiac conditions before visible signs are noticeable to clinical staff, such as atrial fibrillation or premature ventricular contraction (PVC).

## Medical monitor

A medical monitor or physiological monitor is a medical device used for monitoring. It can consist of one or more sensors, processing components, display devices (which are sometimes in themselves called "monitors"), as well as communication links for displaying or recording the results elsewhere through a monitoring network.

a. Components
b. Sensor
c. Sensors of medical monitors include biosensors and mechanical sensors.

## Translating component

The translating component of medical monitors is responsible for converting the signals from the sensors to a format that can be shown on the display device or transferred to an external display or recording device.

## Display device

Physiological data are displayed continuously on a CRT, LED or LCD screen as data channels along the time axis, They may be accompanied by numerical readouts of computed parameters on the original data, such as maximum, minimum and average values, pulse and respiratory frequencies, and so on.

Besides the tracings of physiological parameters along time (X axis), digital medical displays have automated numeric readouts of the peak and/or average parameters displayed on the screen.

Modern medical display devices commonly use digital signal processing (DSP), which has the advantages of miniaturization, portability, and multi-parameter displays that can track many different vital signs at once.

Old analog patient displays, in contrast, were based on oscilloscopes, and had one channel only, usually reserved for electrocardiographic monitoring (ECG). Therefore, medical monitors tended to be highly specialized. One monitor would

track a patient's blood pressure, while another would measure pulse oximetry, another the ECG. Later analog models had a second or third channel displayed in the same screen, usually to monitor respiration movements and blood pressure. These machines were widely used and saved many lives, but they had several restrictions, including sensitivity to electrical interference, base level fluctuations and absence of numeric readouts and alarms.

## Communication links

Several models of multi-parameter monitors are network able, i.e., they can send their output to a central ICU monitoring station, where a single staff member can observe and respond to several bedside monitors simultaneously. Ambulatory telemetry can also be achieved by portable, battery-operated models which are carried by the patient and which transmit their data via a wireless data connection.

Digital monitoring has created the possibility, which is being fully developed, of integrating the physiological data from the patient monitoring networks into the emerging hospital electronic health record and digital charting systems, using appropriate health care standards Medical monitor's embedded software can take care of the data coding according to these standards and send messages to the medical records application, which decodes them and incorporates the data into the adequate fields.

Long-distance connectivity can avail for telemedicine, which involves provision of clinical health care at a distance.

## Other components

A medical monitor can also have the function to produce an alarm (such as using audible signals) to alert the staff when certain criteria are set, such as when some parameter exceeds of falls the level limits.

## Mobile appliances

An entirely new scope is opened with mobile carried

monitors, even such in sub-skin carriage. This class of monitors delivers information gathered in body-area networking (BAN) to e.g. smart phones and implemented autonomous agents.

## Interpretation of monitored parameters

Monitoring of clinical parameters is primarily intended to detect changes (or absence of changes) in the clinical status of an individual. For example, the parameter of oxygen saturation is usually monitored to detect changes in respiratory capability of an individual.

## Change in status versus test variability

When monitoring a clinical parameters, differences between test results (or values of a continuously monitored parameter after a time interval) can reflect either (or both) an actual change in the status of the condition or a test-retest variability of the test method.

## Techniques in development

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The development of new techniques for monitoring is an advanced and developing field in smart medicine, biomedical-aided integrative medicine, alternative medicine, self-tailored preventive medicine and predictive medicine that emphasizes monitoring of comprehensive medical data of patients, people at risk and healthy people using advanced, smart, minimally invasive biomedical devices, biosensors, lab-on-a-chip (in the future nanomedicine devices like nanorobots) and advanced computerized medical diagnosis and early warning tools over a short clinical interview and drug prescription.

## Serotonin biosensor

Future serotonin biosensors may assist with mood disorders and depression.

## Continuous blood test based nutrition

In the field of evidence-based nutrition, a lab-on-a-chip implant that can run 24/7 blood tests may provide a continuous results and a coumputer can provide nutritaion suggestions or alerts.

## Psychiatrist-on-a-chip

In clinical brain sciences drug delivery and in vivo Bio-MEMS based biosensors may assist with preventing and early treatment of mental disorders

## Epilepsy monitoring

In epilepsy, next generations of long-term video-EEG monitoring may predict epileptic seizure and prevent them with changes of daily life activity like sleep, stress, nutrition and mood management.

## Toxicity monitoring

Smart biosensors may detect toxic materials such mercury and lead and provide alerts.

## Lab-diagnostic System or Technology

Computer technology has had a tremendous impact on medical imaging; without computers modern radiological modalities like CT and MRI could not even exist. The interpretation of medical images, however, is still almost exclusively the work of humans. In the next decades this is expected to change. Computers will be used more often for image interpretation. This research area is called Computer-Aided Diagnosis (CAD). All major companies in medical imaging have research labs devoted to CAD and there are a growing number of smaller companies active in the area.

# PHARMACOKINETICS

Pharmacokinetics, sometimes described as what the body does to a drug, refers to the movement of drug into, through, and out of the body—the time course of its absorption, bioavailability, distribution, metabolism, and excretion.

Pharmacodynamics, described as what a drug does to the body, involves receptor binding, postreceptor effects, and chemical interactions. Drug pharmacokinetics determines the onset, duration, and intensity of a drug's effect.

Pharmacokinetics of a drug depends on patient-related factors as well as on the drug's chemical properties. Some patient-related factors (eg, renal function, genetic makeup, sex, age) can be used to predict the pharmacokinetic parameters in populations. For example, the half-life of some drugs, especially those that require both metabolism and excretion, may be remarkably long in the elderly

## PRINCIPLES

A number of medicines in common use have a narrow therapeutic index; that is, the difference between the lowest effective dose and a potentially toxic dose can be quite small. In many cases it is necessary or desirable to undertake therapeutic drug level monitoring (TDM) to ensure that patients can be treated safely. TDM services include the measurement of drug levels in the patient's blood and the application of clinical pharmacokinetics to optimise drug therapy. There is a wide range of medicines that fall into this category, but TDM services typically include amino glycoside antibiotics, anticonvulsants, immunosuppressant, digoxin, lithium and theophylline. Monitoring drug levels in patients can also provide an important indicator as to whether they are taking their medicine. Clinical pharmacy input into TDM services can range from the provision of simple advice to other clinicians on when to take samples and how to interpret results, to fully fledged services that may include collection and laboratory analysis of the blood sample.

**Application** of these principles requires an understanding of the absorption, distribution, metabolism, and excretion characteristics of specific drug products in specific diseases and patient populations. The influence of factors such as age, sex, diet, pathophysiologic conditions, and concomitant use of other drug products must also be understood. The development of patients' individualized dosage regimens should be based on integrated findings from monitoring both the drug

concentration-versus-time profiles in biological fluids and the pharmacologic responses to these drug products. Within the pharmaceutical care process, pharmacists' clinical functions include appropriate and cost-conscious therapeutic drug monitoring and provision of clinical pharmacokinetic assessments. Clinical pharmacokinetic monitoring is necessary when the range between minimal effectiveness and toxicity is narrow and the results of the drug assay provide significant information for clinical decision-making. In the absence of drug concentration measurements, patient-specific characteristics and physiological markers should be used to provide clinical pharmacokinetic assessments and make dosage-regimen recommendations.

## Responsibilities

The following responsibilities should be part of clinical pharmacokinetic services or monitoring conducted by pharmacists:

1. Designing patient-specific drug dosage regimens based on the pharmacokinetic and pharmacologic characteristics of the drug products used, the objectives of drug therapy, concurrent diseases and drug therapy, and other pertinent patient factors (e.g., demographics, laboratory data) that improve the safety and effectiveness of drug therapy and promote positive patient outcomes.
2. Recommending or scheduling measurements of drug concentrations in biological fluids (e.g., plasma, serum, blood, cerebrospinal fluid) or tissues in order to facilitate the evaluation of dosage regimens.
3. Monitoring and adjusting dosage regimens on the basis of pharmacologic responses and biological fluid and tissue drug concentrations in conjunction with clinical signs and symptoms or other biochemical variables.
4. Evaluating unusual patient responses to drug therapy for possible pharmacokinetic and pharmacologic explanations.

5. Communicating patient-specific drug therapy information to physicians, nurses, and other clinical practitioners and to patients orally and in writing, and including documentation of this in the patient's health record.

6. Educating pharmacists, physicians, nurses, and other clinical practitioners about pharmacokinetic principles and appropriate indications for clinical pharmacokinetic monitoring, including the cost-effective use of drug concentration measurements.

7. Developing quality assurance programs for documenting improved patient outcomes and economic benefits resulting from clinical pharmacokinetic monitoring.

8. Promoting collaborative relationships with other individuals and departments involved in drug therapy monitoring to encourage the development and appropriate use of pharmacokinetic principles in pharmaceutical care. Pharmacists with specialized education, training, or experience may have the opportunity to assume the following additional responsibilities:

a. Designing and conducting research to expand clinical pharmacokinetic knowledge and its relationship to pharmacologic responses, exploring concentration–response relationships for specific drugs, and contributing to the evaluation and expansion of clinical pharmacokinetic monitoring as an integral part of pharmaceutical care.

b. Developing and applying computer programs and point-of-care information systems to enhance the accuracy and sophistication of pharmacokinetic modeling and applications to pharmaceutical care.

c. Serving as an expert consultant to pharmacists with a general background in clinical pharmacokinetic monitoring. Readers are referred to ASHP's more thorough publications on the subject of clinical pharmacokinetic monitoring.