

Molecular Imaging Portal: New Development IT Platform for Imaging, Nonimaging and Genomics

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Modern imaging systems such as CT, SPECT, PET, MRI, ultrasound, and others generate a continuously growing amount of clinical and preclinical data every day – easily reaching terabytes in short time periods. In addition, the multiinstitutional and multidisciplinary nature of today's clinical research projects requires the creation of collaborative data repositories with secure, controlled access. Furthermore, data acquired from multimodality imaging platforms should ideally be associated with laboratory and molecular (genomic/proteomic) datasets. In view of the shortcomings of existing commercial systems, the Center for Molecular Imaging Research (CMIR) at Massachusetts General Hospital (MGH) and Siemens have created a new prototype information platform –

the Molecular Imaging Portal (MIPortal). It extends the common PACS functionality beyond radiological imaging and allows storage and query of any type of imaging and data file.

MIPortal is being tested in a heterogeneous academic research environment serving Windows, Unix, and Macintosh clients. Information is organized into projects with secure access based on user privileges. The system is already serving over 40 investigators as a useful tool for collaborative small-animal imaging research and almost one million images have been processed and archived since the beginning of operation.

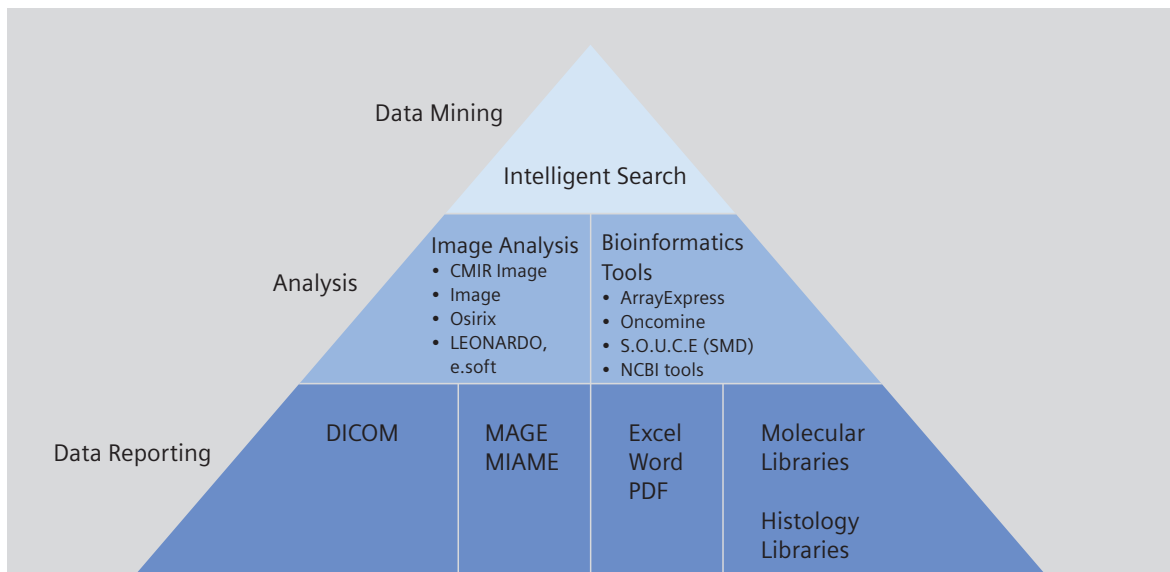
The Challenge: Personalized Medicine

Molecular imaging is a new concept in medicine, combining modern imaging techniques with molecular information such as genomics and proteomics. Information derived from chemical profiling of patients and genetic characterization of cells and excised tissues is already routinely being utilized in various diagnostic fields. However, the integration of such molecular information into patient databases and information management systems is still in its infancy. New approaches in acquiring information about diseases will mostly be driven by molecular imaging, which encompasses new techniques for generating information about the genetic makeup of patients that could become key in improving disease prevention, diagnosis, treatment, and outcome – in other words, personalized medicine. Gene expression profiling and many other genomics and proteomics tools will provide physicians in the future with new disease management options and will have to be introduced into open IT platforms to create a new level of decision support.

To understand the challenges and needs of such a new IT platform, CMIR and Siemens have started a new development project based on IT prototyping within a group of more than 100 researchers working in such a complex environment. The new prototype had to allow for multiplatform imaging integration, storage and management of all imaging/laboratory data, web-based access from different operating systems, and genomics/proteomics data storage and management. Furthermore, search capabilities for internal and external databases were essential for the platform and it was important to provide clinical and preclinical researchers with managing layers beyond the abilities of a standard PACS system. The general concept is depicted in Figure 1.

The Framework: Making Use of Standards

MIPortal is a reliable, web-based prototype system that provides flexible and secure access to complex data generated by more than 15 different modalities. All data is organized in projects and experiments with secure access based on user privileges. Principal investigators can create and own projects and are able to grant access to other MIPortal users. The current system configuration allows data entry either via automated interfaces based on industry standards or manually by investigators. ▶



(Figure 1)

The general pyramidal concept of the MIPortal platform. The foundation of the pyramid displays the data repository aspect of the concept with storage capabilities for imaging (DICOM), genomics (MAGE, MIAME), laboratory data (Excel, Word, PDF, etc.), and other databases such as molecular

libraries and non-DICOM imaging databases (tif, jpg, etc.). The middle layer represents the integration of image analysis and bioinformatics tools (genomics/proteomics), followed by the top layer of intelligent data mining of all information.

The web-based nature of the user interface makes it easy for users to adopt the system, as it has no requirements for proprietary software to be installed on the client's computer. System access is available for authorized users, regardless of their physical location, via the Internet. CMIR utilized an existing institutional infrastructure – MGH Partners Network – for VPN-encrypted communication. In addition, the browser-based user interface provides a familiar look and feel for the preclinical user and significantly minimizes training requirements for new users.

To avoid reinventing existing software and hardware solutions for imaging and nonimaging data, the prototype was built upon adopted and emerging standards. The DICOM format was accepted as the common standard for clinical imaging and therefore all imaging modalities with DICOM-formatted imaging output can

store it directly on a clinical PACS system. Non-DICOM imaging modalities, such as most optical fluorescence-based systems and microscopy, can be stored in their original image formats. However, the images can also be converted to DICOM, utilizing a proprietary DICOM converter through the MIPortal interface. The multi-platform nature of the web-based user interface allows the use of a DICOM converter with any modality (250 000 images converted to date). For example, Macintosh-operated microscopes provide direct access to the converter through the MIPortal web interface (visualized in Safari), enabling translation and transfer of images to the storage environment while in operation.

The Platform

The MIPortal is a four-tier application. The basic system encompasses four different server platforms on top of a flexible PACS system. A small PACS server with a

Siemens MagicView 300 and DVD jukebox provides clinical DICOM compatibility and allows for direct storage of images coming from DICOM-output-configured modalities. Other PACS platforms, such as the MGH PACS servers, can easily be linked. A standard Microsoft IIS web server provides the integration of the Microsoft .NET framework. The application server extends the functionality of the Siemens *syngo*[®] platform, which is used across all Siemens modalities, to the web. The Microsoft .NET architecture allows for the seamless integration of the *syngo* Front End (FE) and browser-based .ASP layers. The integrated database server utilizes an Oracle 9.2 database engine; however, image files are not stored as binary objects directly in the database. Instead, files are placed on a file system with pointers kept in the database. Log-in information, user preferences, and access rights are also driven by relational database tables, which make the MIPortal much less platform dependent. The back-end server is responsible for interfacing with modalities. It provides a secure communication infrastructure as well as validation of incoming data. If the data does not conform to a protocol, it is referred back to an acquisition modality for correction to create a feedback process for validation. This ensures consistency and uniformity of image data in the MIPortal. The basic components of the system are illustrated in Figure 2.

A fundamentally different model applies to research in contrast to clinical applications. These projects usually have a much longer lifetime, meaning that data needs to be available on-line and must remain directly accessible for a much longer timeframe than clinical images. A DVD or tape storage solution is required, but large on-line storage capabilities need to be added for interactive data access. The MIPortal therefore also incorporates Network-Attached Storage (NAS) functionality with multiple terabyte on-line disk space accommodating all data of all active projects.

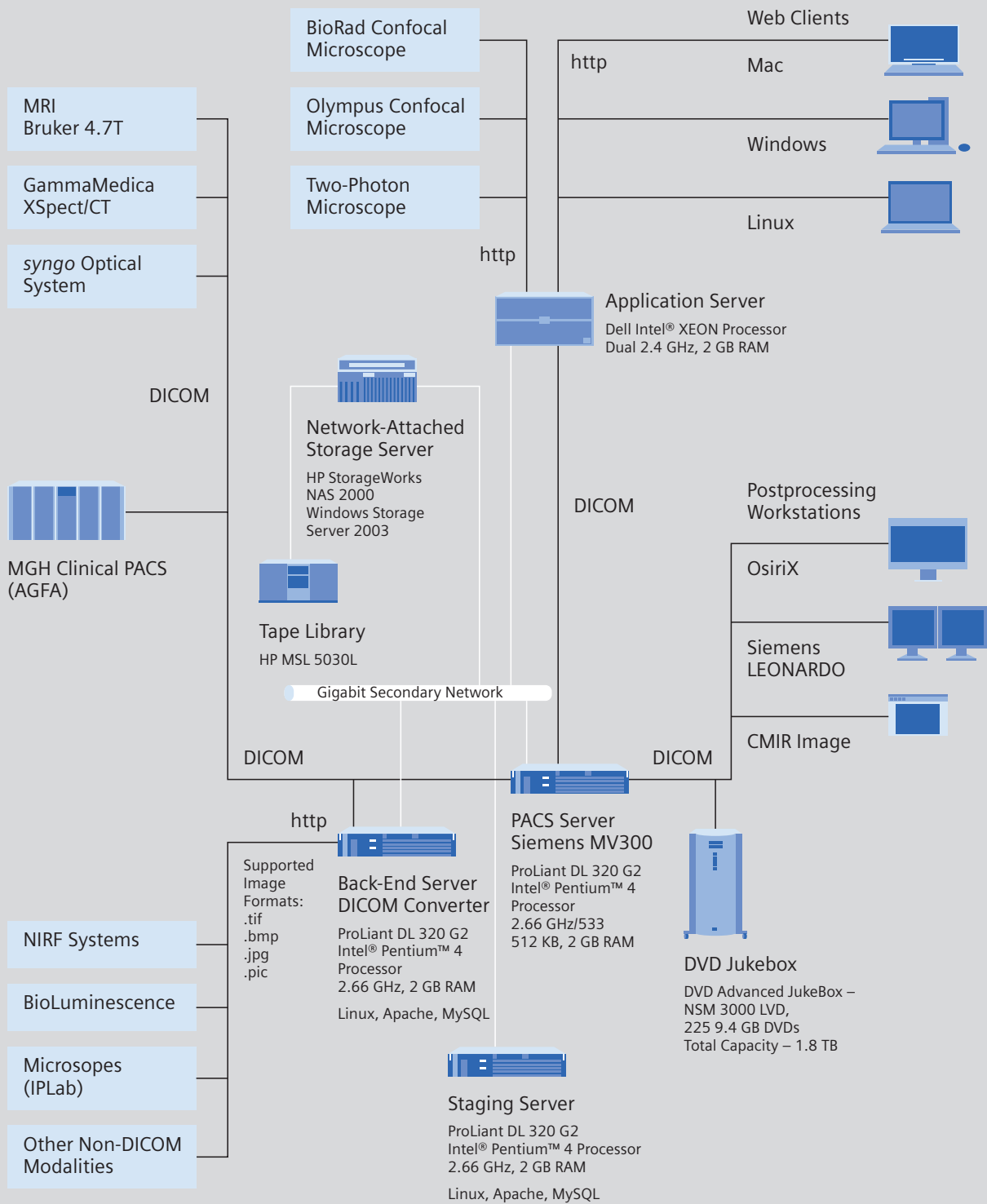
The standard DICOM data model was also extended to reflect conditions typical for a research environment. Unlike patient-centric clinical environments, research laboratories organize data in an experiment- or project-centric model. Name or medical record number most often cannot identify subjects of experiments, which can be translated directly into the clinical environment. The new model structure adds the functionality to

flexibly perform an experiment based on tissues, animals, or phantoms. Furthermore, in the course of performing an experiment, a multitude of data files is generated. A project plan, a PowerPoint or Keynote presentation, Excel spreadsheets with measurement results, cluster analysis heat maps, or virtually any conceivable data file can be a part of an experiment. A new mechanism was required to add such data files to an experiment or a project. The MIPortal allows a user with read-write access to upload any file, using a browser-based form, and to organize all relevant information related to the project. Different types of users can be defined and given access to data either within projects or across projects, restricted to certain information or data type. The screen for defining users is shown in Figure 3, the screen of the DICOM converter is displayed in Figure 4.

Multiphased Approach and Current Functionality

CMIR and Siemens decided to implement various consecutive phases for the MIPortal development. The initial phase included the installation of the small PACS system MagicView 300 with a 2.3-terabyte jukebox following a standard online data storage model. All DICOM modalities are connected to the PACS server and a web client developed to provide operating system-independent access to the PACS server. In the successive phase, non-DICOM modalities are integrated through DICOM conversion tools as well as a project management layer, created to allow advanced and complex data management for all users. All phases are generated and implemented by Siemens Medical Solutions in interim releases to allow testing of individual steps by the multiuser environment of CMIR.

During the implementation and testing phases, users found it increasingly important to be able to search the new system for information characterizing specific experiments. Despite the fact that the data was organized in projects and experiments, it was not always easy to find a particular piece of information. This issue became especially relevant with the rapid growth of the MIPortal repository and was solved by implementing an extensive search functionality developed especially for the MIPortal infrastructure. In fact, two distinctly different but complementary functions were developed – Quick Search and Power Search. Quick Search allows



(Figure 2)

Schematics of the individual components of the MIPortal. Four servers with different functions are connected through a high-speed intranet network and linked to a PACS server with a DVD jukebox. DICOM modalities and other PACS systems access the MIPortal through the DICOM server. Non-DICOM modalities enter the network first through the backend server with DICOM converter. Postprocessing image workstations are linked through the standard network with the PACS server, while some modali-

ties and all PCs are routed through the applications server (the actual location of the MIPortal). A NAS server is utilized to keep all data on-line and provides backup capabilities for imaging and nonimaging data (DVD jukebox only stores DICOM). The standard user gains access to the MIPortal through the applications server. The integration of bioinformatics tools, access to genomics and proteomics information, and intelligent search capabilities are also provided by the applications server.

a Google-style keyword search of the entire database. It returns a list (or a hierarchy) of projects, experiments, documents, and DICOM structures that produces a hit for each keyword. It is fast, convenient, and accessible on every page. However, results are not always sufficiently precise to reduce the number of hits. Power Search allows users to specify search criteria on a more granular level. For instance, a specification of experiment date, investigator name, and patient MRN is possible. Both searches have proven to be extremely useful to novice and experienced users alike.

The MIPortal prototype has operated successfully for 18 months and has proven to be an indispensable tool for organizing and distributing heterogeneous data generated at the CMIR. Internal investigators as well as external collaborators have adopted it and utilize it on a daily basis. Siemens plans to install the MIPortal at additional beta sites for further extensive testing of its functionality and capabilities in preclinical and potentially clinical settings. It is a simple yet powerful system for information storage and exchange. At the moment there are 39 active users and over 953 000 images of 19 different modalities on-line and parts of 51 active projects, 40 completed projects, and 441 experiments. The system is currently maintained by only one person, committed part time (25%), which illustrates the system's ease of use.

Genomics and Proteomics Integration

The next phases of this prototype development IT platform were focused on two areas: first, the integration

of image-handling tools commonly used with PACS systems, and secondly, the storage as well as viewing of genomics/proteomics data. CMIR and Siemens decided to begin this approach with the implementation of micro array data utilizing the MAGE standard for genomics, similar to the previous approach utilizing DICOM as the imaging standard. Siemens was able to employ early in-house developments of genomics developments created within Siemens Corporate Technology to accelerate the process of genomic software integration into the MIPortal. GeneSim can be best described as a prototype software platform that allows the storage and analysis of extensive micro array data and gene expression profiling. Siemens is currently adapting and implementing the storage and retrieval components into the MIPortal, followed by enabling viewing capabilities and establishing links to genomic analysis software. These steps represent the initial phases of the integration of complex molecular information that is needed for the assessment of diseases and are key features for the personalization of medicine and healthcare.

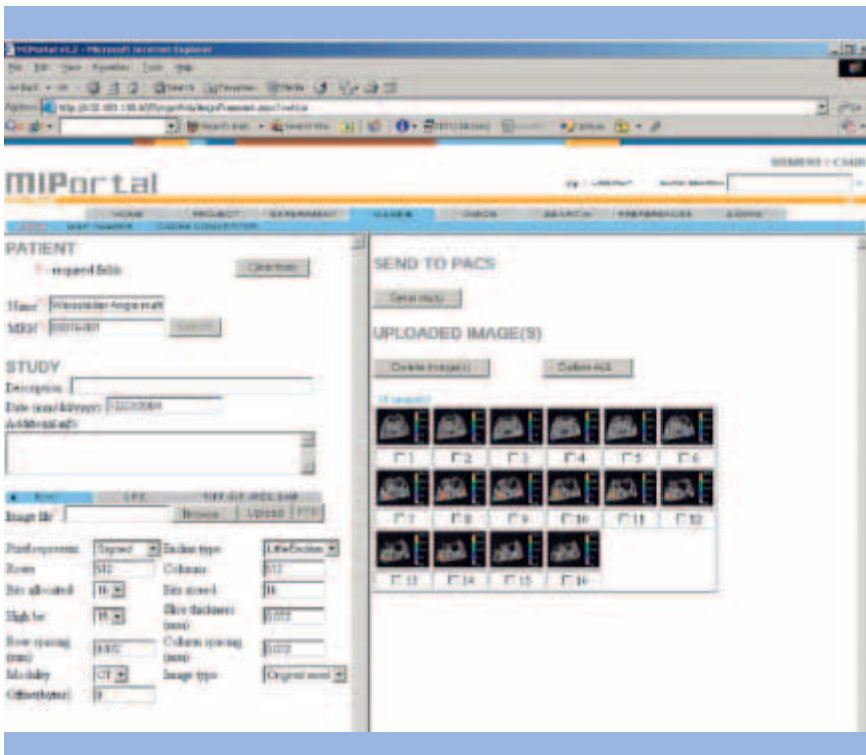
Future Developments and Outlook

In less than one year of operation and prototyping, the MIPortal has become an essential tool for molecular imaging research. Its most successful features are the project-oriented organization of the platform, the growing number of incorporated modalities through the adaptive DICOM converter, Internet access from any operating system using Internet Explorer, and the ability to store any document related to the defined



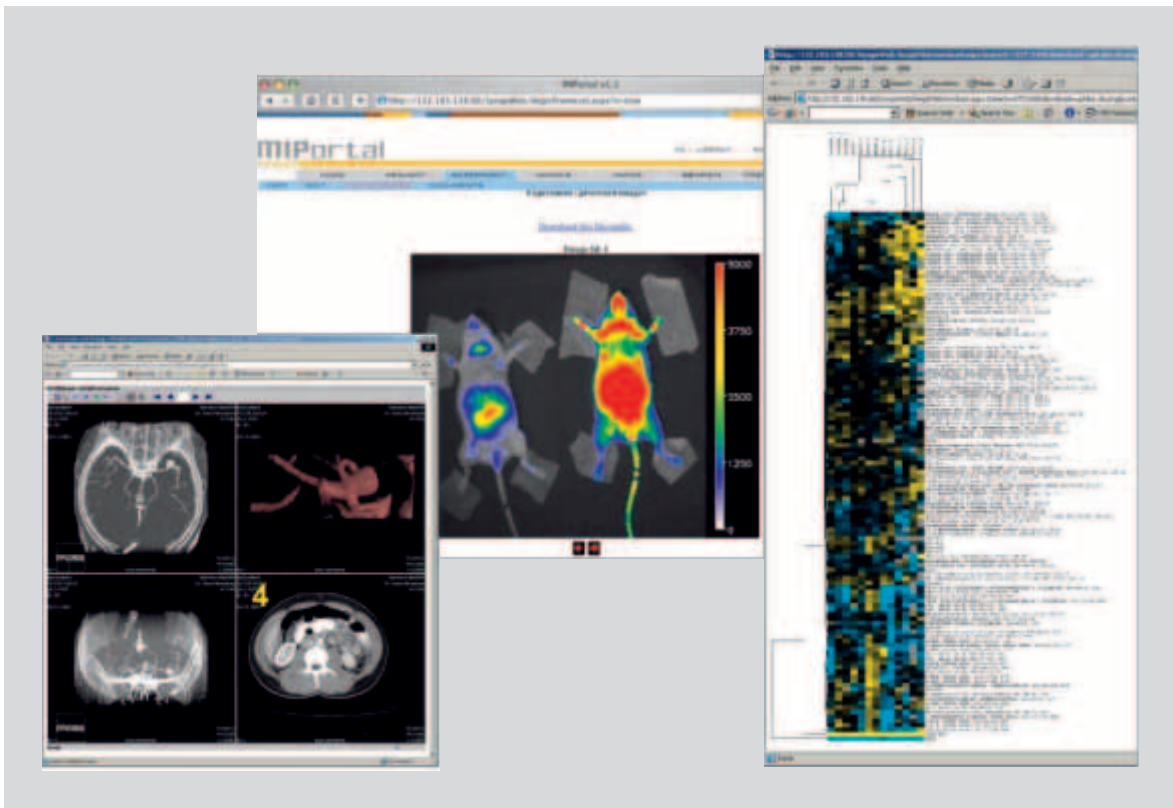
(Figure 3)

Web-based screen for defining users and user rights as seen in Safari on a Macintosh computer. Name and personal parameters can be defined. The MIPortal administrator can then define the user's access rights to projects and data. Every account is also password protected.



(Figure 4)

Web-based screen for utilizing the DICOM converter as seen in Internet Explorer on a Windows computer. Any image can be uploaded as a DICOM file into the PACS system, if standard DICOM conventions are applied. The converter currently allows the conversion of images from optical imaging systems, light and fluorescence microscopy, and even histology, if required.



(Figure 5)

Web-based screens of typical data analysis platforms utilized together with the MIPortal. Whether it is clinical imaging analysis using syngo capabilities, optical imaging software for preclinical

imaging, or genomics screening and gene sequence analysis, all of these tools can be combined with the data retrieval and storage of the MIPortal.

project. Furthermore, all existing and new software can be utilized for the analysis of the data generated, since the MIPortal web interface can be accessed from any computer (Windows, Linux, Macintosh, etc.) while acquiring data or performing analyses. After the successful integration of micro array data formats and other genomics/proteomics data formats, CMIR and Siemens will focus on intelligent data mining, utilizing the MIPortal for the development of new diagnostic tools combining imaging, nonimaging, and genomic databases. However, at its current stage, the MIPortal has great potential to become the key platform for preclinical research at universities and pharmaceutical laboratories. After adding compliance with legal requirements, it may

also allow the organization of clinical trial data, which has been shown to have great potential in early test case studies with small clinical trials at CMIR.

WIP – the information about this product is preliminary. The product is under development and is not commercially available in the U.S., and its future availability cannot be ensured.

E/E

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