# A Multidisciplinary Approach to Honest Broker Services for Tissue Banks and Clinical Data

## *A Pragmatic and Practical Model*

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**BACKGROUND.** Honest broker services are essential for tissue- and data-based research. The honest broker provides a firewall between clinical and research activities. Clinical information is stripped of Health Insurance Portability and Accountability Act-denoted personal health identifiers. Research material may have linkage codes, precluding the identification of patients to researchers. The honest broker provides data derived from clinical and research sources. These data are for research use only, and there are rules in place that prohibit reidentification. Very rarely, the institutional review board (IRB) may allow recontact and develop a recontact plan with the honest broker. Certain databases are structured to serve a clinical and research function and incorporate 'real-time' updating of information. This complex process needs resolution of a variety of issues regarding the precise role of the HB and their interaction with data. There also is an obvious need for software solutions to make the task of deidentification easier.

**METHODS.** The University of Pittsburgh has implemented a novel, IRB-approved mechanism to address honest broker functions to meet the specimen and data needs of researchers. The Tissue Bank stores biologic specimens. The Cancer Registry culls data and annotating information as part of state- and federal-mandated functions and collects data on the clinical progression, treatment, and outcomes of cancer patients. The Cancer Registry also has additional IRB approval to collect data elements only for research purposes. The Clinical Outcomes Group is involved in patient safety and health services research. Radiation Oncology and Medical Oncology provide critical treatment related information. Pathology and Oncology Informatics have designed software tools for querying availability of specimens, extracting data, and deidentifying specimens and annotating data for clinical and translational research. These entities partnered and submitted a joint IRB proposal to create an institutional honest broker facility. The employees of this conglomerate have honest broker agreements with the University of Pittsburgh and the Medical Center. This provides a large group of honest brokers, ensuring availability for projects without any conflict of interest.

**RESULTS.** The honest broker system has been an IRB-approved institutional entity at the University of Pittsburgh since 2003. The honest broker system currently includes 33 certified honest brokers encompassing the multiple partners of this system. The honest broker system has handled >1600 requests over the past 4 years with a 25% increase in volume each year.

**CONCLUSIONS.** The current results indicate that the collaborative honest broker model described herein is robust and provides a highly functional solution to the specimen and data needs for critical clinical and translational research activities.

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**KEYWORDS: honest broker, biologic specimens, data annotation, Institutional Review Board, tissue bank, translational research, Health Insurance Portability and Accountability Act of 1996.**

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The last decade has seen significant advances in molecular biology (genomics and proteomics) and translational research. These new initiatives have resulted in a growing demand for specific, highly annotated human tissues and other biologic specimens.[1-3] This growing demand has reinforced the importance of tissue banks as a major part of the necessary infrastructure of any institution/research initiative seeking to address biologically and clinically relevant issues.[4-6] The National Cancer Institute has an office dedicated to biospecimens[7] that has provided a document detailing best practices for repositories.[8] In addition, the International Society for Biologic and Environmental Repositories has put together a 'best practices' document that incorporates suggestions from its members.[9] Similar initiatives have been undertaken in the US[2] and the UK.[10] Finally, there are variations of laws from state to state regarding the use of tissues and annotating data.[11] In addition, many of these research initiatives require extensive annotating information that is not present in a single data source.

Two areas particularly need annotating information. These are tissue-based research and health services-based research, which requires patient information for research assessment. Health services research includes outcomes-focused research, assessing the impact of different therapeutic regimens, research focused on quality and safety of healthcare, research to evaluate quality assurance, quality control and errors, and research focused on the impact of different information systems on overall quality of health delivery, patient education, and error reduction.

The past few years also have witnessed a significant structured movement to protect the confidentiality of research study participants. Although the concept of an honest broker has been around for more than a decade, the advent of the Health and Insurance Portability and Accountability Act of 1996 (HIPAA)[12] further emphasized the need for systems/mechanisms to identify and remove personal health identifiers (PHIs) from research information. It should be noted that HIPAA does not address research information, except that it may become a PHI if it is identified and in a covered entity. There are facility/institution-specific regulations mandating policies on patient confidentiality. The Institutional Review Board (IRB) also provides input and direction regarding policies and procedures that have an impact on access to patient information. Finally, institutions also are cognizant of prevailing views regarding legal and ethical issues. It is important to develop protocols to protect patient identifiers and confidentiality in the current environment.

The need for data as well as the need for patient confidentiality protection resulted in a log jam blocking data aggregation and disbursement. This conflict exposed the lack of preparedness of major institutions to collect, collate, and disburse data elements needed for projects while maintaining patient privacy. The result was that access to well documented tissue specimens using normalized descriptors became an important impediment to the progress of research projects.[13]

At the University of Pittsburgh, the Cancer Registry and the Health Sciences Tissue Bank engaged in discussions to evaluate mechanisms for addressing this issue. The major players in the research field were identified. The Health Sciences Tissue Bank, the Pathology Laboratory Information System, the Cancer Registry, the Clinical Research Informatics Service, the Clinical Outcomes Group, Radiation and Medical Oncology, Pathology and Oncology Informatics, and the 'Electronic Medical Record' team were considered key players. This list may not encompass every possible entity that could play a role; nonetheless, it captures the major players involved in the aggregation and provision of specimens and data. Policies and procedures were established to serve as guiding principles.

## MATERIALS AND METHODS

Requests for biologic specimens and data for research purposes have increased significantly over the years. Data requests have become increasingly complex. This increased complexity is associated in part with outcomes-related initiatives to evaluate biomarkers and their role in guiding therapy or predicting outcomes. In addition, awareness of confidentiality issues has increased significantly since the implementation of HIPAA. The primary request for research projects consist primarily of 1) tissue and biologic specimens only; 2) clinical (phenotype) data, most frequently pathology data; and 3) outcomes information, including treatment, progression, and vital status.

We evaluated tissue and data requests at the University of Pittsburgh and observed that 20% of research projects needed biologic specimens only, 10% of research projects needed outcomes information, and the remaining 70% needed more fully annotated tissues that required phenotypic (clinical) data. The annotation varied from easily accessible (eg, pathology data) to complex (pretherapy and post-therapy information). This breakdown of research requests is shown in Figure 1. These findings suggested the need to design a system that could provide research biologic specimens annotated with patient data while protecting the confidentiality of patient information and fully meeting the requirements of federal regulations.[14] This would require the implementation of a system that was HIPAA compliant and provided protection for human participants. The resulting system for this process was based on the honest broker concept.

In many instances, the collection of information on clinical progression, treatment, and outcomes of cancer

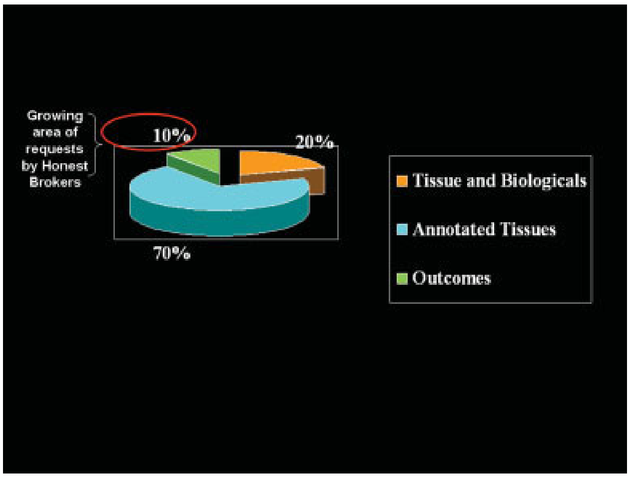


**FIGURE 1.** Breakdown of research requests received and their associated annotation requirements.

patients may fall under the rules for 'human subjects' research and, thus, require specific IRB review and approval. The overall attempt is to obtain 'informed consent' from all patients for research use of their biologic materials. In addition, the various registries at the institution attempt to obtain 'informed consent' from all patients for the research use of their data.

### Human Subjects Protection—The Honest Broker Concept

The tissue/databank ensures protection of patient identity through the 'honest broker' concept. The honest broker is an individual/organization/system that acts for or on the behalf of the tissue/databank. The role of the honest broker is to collect and provide health information to research investigators in such a manner that it would not be reasonably possible for the investigators or other individuals to identify the patients directly or indirectly. The 'honest broker' or 'tissue/data bank trustee' acts as a well defined barrier between the clinical environment (in which fully identified, confidential patient information is exchanged routinely as part of medical care) and the general research community (in which all information must be deidentified completely). The honest broker also ensures that research data, which generally are not validated clinically, are not used for clinical care.[15]

In our rendition, the honest broker is not part of either the clinical or research team. The honest broker is dedicated to providing 'honest broker' services only to a particular project and is not part of either the data collection team or the research team. This is to avoid any potential conflict of interest. It needs to be emphasized that these roles change from project to project for a particular individual. However, the end result is that the dedicated honest broker for that project is not part of either the research team or the data/biologic specimen aggregation team.

This is important to ensure confidentiality and honest research. The honest broker is the only entity that can link research identifiers and clinical identifiers. This transfers control and responsibility of the deidentification process to an independent third party, the honest broker, thereby reducing the risk of conflict of interest. Personal and clinical identifiers (names, addresses, medical record numbers, etc) are limited to the clinical space. The research identifiers (ie, 'Subject 12,432') cannot be traced back to the personal or clinical identifies except through the honest broker's linkage codes.

This concept differs from anonymization, which is a 1-way process in which the linkage between personal identifiers and research identifiers is removed. Anonymization precludes any subsequent updating of data. The process of data annotation with the particular specimen stops when anonymization is performed. The process of having the honest broker assign linkage codes (reidentification codes) allows information to be updated at anytime in the future. The honest broker can identify the patient by means of the linkage code, access information related to this patient from the clinical domain, and provide updated information to the researchers in a deidentified fashion using the original linkage code. The link between codes must be retained and protected by the honest broker. Subsequent requests to update information on research protocol participants (research cohort) must be conducted through the honest broker. Therefore, the honest broker system is an upgrade to the process of anonymization. Anonymization essentially provides information up to the time of accrual, whereas the honest broker concept allows information to be updated in a manner that is consistent with current legal and ethical protocols.

Discussions involving the Cancer Registry and the Health Sciences Tissue Bank identified the major sources of tissue and biologic specimens and annotating data for research use. The privacy rule of HIPAA permits access to protected health information without patient authorization in a limited number of situations.[12] One frequent situation is when the protected health information is being used in a deidentified fashion. The honest broker plays a prominent role in this scenario, because neither the federal policy nor HIPAA regulations require prior written consent or authorization of patients when using existing health information in a deidentified fashion. The honest broker can be a part of the facility providing the data. In addition the honest broker can be a business associate of the facility.[16] Supplemental files included the University of Pittsburgh template business associate agreement. This approach allowed us to expand the circle of participating facilities. We decided to include divisions/departments involved in data aggregation as well as facilities that were creating and implementing software solutions and tools for these groups as participants for this initiative. The software groups included Pathology and Oncology Informatics and the Electronic Medical Records team. This list may not include every possible entity that could play a role; nonetheless, it does capture the major players involved in the aggregation and provision of specimens and data and in designing software tools for these efforts. The facilities that currently are part of the 'Honest Broker Facility' and their roles in this initiative are described below.

## Participating Facilities

### *The Health Sciences Tissue Bank*

The Health Sciences Tissue Bank is the main institutional infrastructure for collecting tissue and other biologic materials for research. These research specimens are stored in a deidentified fashion and annotated with linkage codes because of confidentiality issues. However, the linkage codes allow access to specific information regarding the donor. This is important because many research projects require not only tissue and biologic specimens but also additional data regarding family history, treatment history, and outcomes.

### *The Pathology Laboratory Information System*

This is the clinical system used for reporting pathology information. This repository contains extensive information regarding clinical evaluation of tissue and other biologic specimens. This information is extremely useful to provide a better understanding of the composition of the research specimen. The system stores clinically reported information pertaining to tissue specimens (biopsy and resection reports), cytology specimens (exfoliated as well as aspirate specimens), and other biologic specimens (blood, blood products, urine, other biologic specimens).

### *The Cancer Registry*

The Cancer Registry performs the state-mandated function of collecting information on cancer patients. The information collected pertains to both diagnostic details as well as follow-up information. The data collected by the registry consists of a set of defined data elements that are part of a standardized set of common data elements. We have modified this approach further by adding additional data elements of primarily research value as part of a separate IRB-approved initiative.

### *The Clinical Outcomes Group*

This institutional entity collects and provides information pertaining to ongoing clinical trials, health services research, and patient safety research.

### *Radiation and Medical Oncology*

Radiation and Medical Oncology are important caregivers for oncologic diseases. The clinical database of these 2 entities provides critical information regarding therapeutic intervention and responses to those specific therapies. Information accrued from Radiation and Medical Oncology, thus, is critical for providing insight regarding patient response to therapeutic protocols.

### *Pathology and Oncology Informatics*

The Pathology and Oncology Informatics division is responsible for designing and maintaining the informatics infrastructure for the collection, storage, and disbursement of annotating information. It is important to affiliate this group with developing the honest broker infrastructure, because Pathology and Oncology Informatics designs, tests, and maintains the tools needed for the other components of the honest broker system. Some of these include software packages needed for inventory management by the Health Sciences Tissue Bank, data aggregation software packages for the Cancer Registry and Clinical Outcomes Group, clinical information and research information recording mechanisms for Medical and Radiation Oncology, and deidentification software packages needed by many participating facilities (Health Sciences Tissue Bank, Cancer Registry, the Electronic Medical Record Team, and others). It is noteworthy that our Pathology and Oncology Informatics groups recently were merged into the new Department of Biomedical Informatics as of June 2006 (available at: http://www.dbmi.pitt.edu accessed on July 23, 2008).

### *The University of Pittsburgh Health Systems Information Services Division*

Most clinical data are captured in an electronic form in various hospital information systems. This includes patient history, details of surgical and radiologic procedures, therapeutic interventions, and follow-up information. The clinical component of the electronic medical record consists of information in an identified form. However, the transfer of this information into the research domain requires deidentification. The Electronic Medical Record Team, therefore, serves as a gatekeeper for this information and oversees the implementation of appropriate deidentification protocols before the incorporation of these data into research databases. The electronic Medical Record Team also plays a critical role in performing queries for specific research requests. This activity helps identify appropriate patient populations for research projects. These identified patient lists then need to undergo deidentification.

In this concept, at least 1 individual is acting as an honest broker at each of the facilities described above.

For clinical and translational research studies in oncology, the cancer registrars are extremely valuable because their federal mandate and job specifications allow them ready access to clinical information on cancer patients. In addition, they are not involved in specimen banking or research and, thus, do not have access to the data annotating tissue bank samples or the results of the research studies. The inclusion of the Cancer Registry into an honest broker system facilitates data accrual from this purely clinical data entity, which maintains updated information on all oncology patients. This updating is done every 6 months and is part of the state-mandated function of the Cancer Registry.

The 'institutional honest broker' system ensures that the honest broker ('trustee') is the only individual who can link a patient with the tissue bank number that identifies that patient. The institutional honest broker system also provides a process through which new clinical outcome information can be added to a file that is identified only by a code number rather than a name. This creates a fail-safe mechanism for communicating with patients in the extremely rare event of an IRB-directed dissemination of important research data to the patient or their survivors. It was decided to incorporate the entities described above, which are involved in tissue and data aggregation with possible research application, into an institutional honest broker system.

The University of Pittsburgh Academic Health Center consists of 2 closely interacting, but legally separate, entities. These are the University of Pittsburgh, which oversees primarily the research activities, and the University of Pittsburgh Medical Center (UPMC), which oversees clinical activity and in which the clinical data resides. Potential legal/ethical issues pertaining to the creation of this system were discussed with the IRB of the University of Pittsburgh as well the legal team of the UPMC. A formal IRB application for this 'Honest Broker Facility' incorporating the comments and suggestions of the IRB and the legal team of the UPMC Health Systems was approved by the IRB and formally went into effect on May 8, 2003.

The employees of the Honest Broker Facility have honest broker agreements with the University of Pittsburgh and the University of Pittsburgh Health Systems. This Honest Broker Facility encompasses several separate departments and divisions. Each of these entities has contributed by providing personnel into the honest broker pool. This arrangement has provided a large task force for honest broker activities, which is important because an honest broker should not be involved with research that requires honest broker services. This approach ensures lack of conflict for the individual engaged in honest broker activities, thereby creating an appropriate work environment.

## Honest Broker Process

The honest broker certification process requires the completion of IRB-mandated education modules. These modules are Research Integrity, Human Subjects Research in Biomedical Sciences, and HIPAA Researchers Privacy Requirements. The education modules can be completed online at the University of Pittsburgh IRB website (available at: http://cme.hs.pitt.edu/ accessed on July 23, 2008). A certificate of completion is generated once each module has been completed. In addition, the honest broker has to enter into a business associate agreement.[16] An individual can become a Certified Honest Broker once these administrative requirements have been completed.

The Honest Broker Facility provides an update to the IRB every 6 months. The update is in opportunity to add/delete honest brokers. The Institutional Honest Broker System at the University of Pittsburgh has assigned overall administrative responsibility for the honest broker service to the manager of the Cancer Registry. However this oversight can be provided by the leaders of any of the participating entities.

The Pathology and Oncology Informatics division has designed a Data Request Tracking Tool for the honest broker system. This tool is located on a password-protected website. The description of the process and interaction with affiliated entities is described on an accessible website (available at: http://www.upci.upmc.edu/facilities/cis/serv.html accessed on July 23, 2008). This tool provides the interface for entering descriptive detail information pertaining to a research project that requires honest broker services. This tracking tool is password protected and is located within the firewall of the University of Pittsburgh. After logging onto the system, a menu of options is available to the honest broker. This is shown in Figure 2. The honest broker who is handling a particular request enters all information regarding the research project into the database using the initial data-entry screen of this tool. The initial data-entry screen captures information pertaining to the investigator, the nature of the request, and important workflow issues, such as requested turnaround time, IRB status, and approval number. In addition, this screen captures information pertaining to billing in case the services provided will be compensated through an institutional account rather than through grant-funded mechanisms. This tool has a built-in query capability. The honest broker designates the fields required for the data sources, the disease category, the method of output for tissue/biologic specimens and data, the method of distribution, and the purpose of the request. A screen capture of this aspect of the tool is shown in Figure 3. The honest broker alerts their supervisor once all project information has been entered into the tracking tool. The supervisor reviews project details and provides input and approval. This tracking tool is

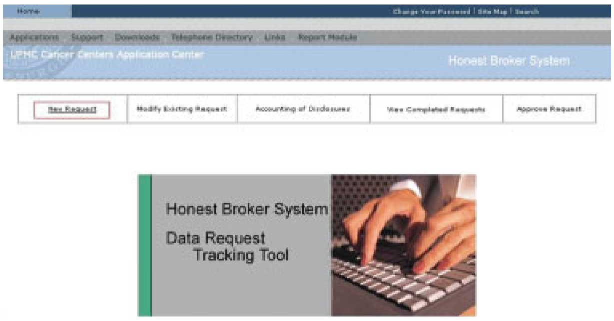
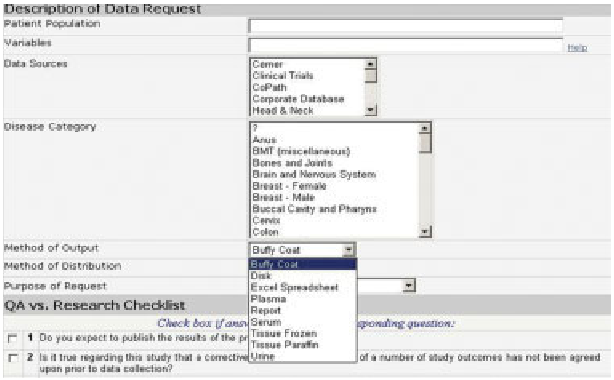


**FIGURE 2.** A screen capture of the login screen for the Honest Broker tool. It shows the multiple processes involved in serving a request by the Honest Broker.



Description of Data Request

Patient Population

Variables

Data Sources: Cerner, Clinical Trials, CoPath, Corporate Database, Head & Neck

Disease Category: ?, Anus, BMT (miscellaneous), Bones and Joints, Brain and Nervous System, Breast - Female, Breast - Male, Buccal Cavity and Pharynx, Cervix, Colon

Method of Output: Buffy Coat

Buffy Coat, Disk, Excel Spreadsheet, Plasma, Report, Serum, Tissue Frozen, Tissue Paraffin, Urine

Method of Distribution

Purpose of Request

QA vs. Research Checklist

*Check box if answ… …sponding question:*

☐ 1 Do you expect to publish the results of the pr…

☐ 2 Is it true regarding this study that a corrective… of a number of study outcomes has not been agreed upon prior to data collection?

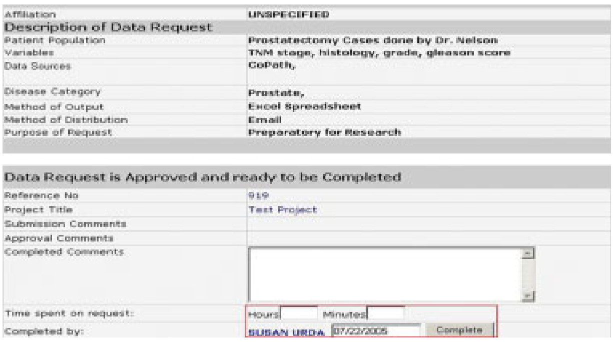
**FIGURE 3.** A screen capture of the query tool showing the multiple types of data and biologic specimen requests that it can handle.

used to follow a research tissue/data request from start to finish. This provides information regarding turnaround time as well as time spent on a project. All of this information is summarized and available in the final 'complete request' snapshot of the tool, which is shown in Figure 4.

## Deidentification Protocols

The deidentification of patient samples and data is performed by using a variety of tools. The Pathology Laboratory Information System, CoPath, has limited deidentification capabilities. The Electronic Medical Record system also has deidentification software systems. The honest broker system can be used for deidentifying specimens/data, with the honest broker retaining codes for the specimen/data provided. The Clinical Research Informatics Service (available at: http://www.dbmi.pitt.edu/cris/ accessed on July 23, 2008) in the Department of Biomedical Informatics has created an HIPAA-compliant deidentification engine. Electronic mechanisms for addressing honest broker issues are described in the literature.[17-19]

This deidentification engine has been certified by the IRB of the University of Pittsburgh and by the UPMC security office for generating deidentified output from a variety of free text medical reports. This engine identifies all HIPAA-mandated PHIs, eg, it names and replaces them with a deidentified tag and replacement letters. If the same individual is encountered in multiple places in the same report, then the same replacement letters are used for every occurrence. Similarly, dates are replaced by an offset, which allows intervals among aggregated reports to still allow for interval determination. An example of a deidentified report generated by this engine is shown in Figure 5. The system generates a linkage file for each patient. This file is stored on a secure server. A diagram representing this process is shown in Figure 6.



| | |
|---|---|
| Affiliation | UNSPECIFIED |
| **Description of Data Request** | |
| Patient Population | Prostatectomy Cases done by Dr. Nelson |
| Variables | TNM stage, histology, grade, gleason score |
| Data Sources | CoPath, |
| Disease Category | Prostate, |
| Method of Output | Excel Spreadsheet |
| Method of Distribution | Email |
| Purpose of Request | Preparatory for Research |
| **Data Request is Approved and ready to be Completed** | |
| Reference No | 919 |
| Project Title | Test Project |
| Submission Comments | |
| Approval Comments | |
| Completed Comments | |
| Time spent on request: | Hours Minutes |
| Completed by: | SUSAN URDA 07/22/2005 |

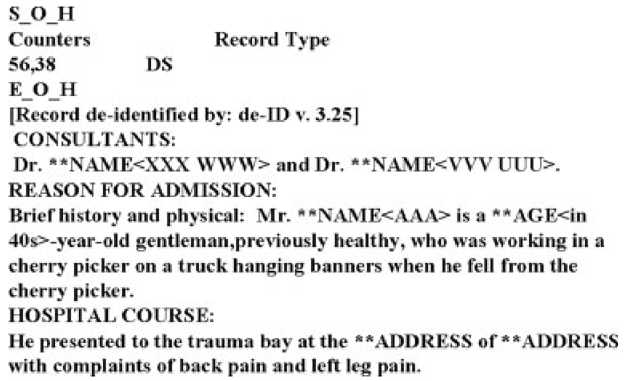
**FIGURE 4.** This screen capture shows the 'completed request' summary generated by the Honest Broker tool.

## Data Sources

The collaborative honest broker service uses multiple sources of data. These include clinical applications (Pathology Laboratory Information Services, Radiation Oncology Systems, Outpatient Systems, and Hospital Information Systems), clinical trials-related applications, Cancer Registry applications, and tissue banking inventory and information systems. In addition, paper-based records in physician offices and legacy records in the hospital may be used. These multiple data sources are listed in Figure 7.

## Oversight of the Honest Broker System

Sharon Winters, the director of the Cancer Registry, serves as the overall manager of the Honest Broker Facility. She is responsible primarily for maintaining oversight regarding administrative and regulatory issues. She is assisted in this role by the lead supervisors of the participating facilities. These include the manager of the Tissue Bank, the manager of the Quality Assurance facility, the manager of Pathology and Oncology Informatics,



S_O_H
Counters Record Type
56,38 DS
E_O_H
[Record de-identified by: de-ID v. 3.25]
CONSULTANTS:
Dr. **NAME<XXX WWW> and Dr. **NAME<VVV UUU>.
REASON FOR ADMISSION:
Brief history and physical: Mr. **NAME<AAA> is a **AGE<in 40s>-year-old gentleman,previously healthy, who was working in a cherry picker on a truck hanging banners when he fell from the cherry picker.
HOSPITAL COURSE:
He presented to the trauma bay at the **ADDRESS of **ADDRESS with complaints of back pain and left leg pain.

**FIGURE 5.** An example of a deidentified report created by the 'Deidentification' engine.

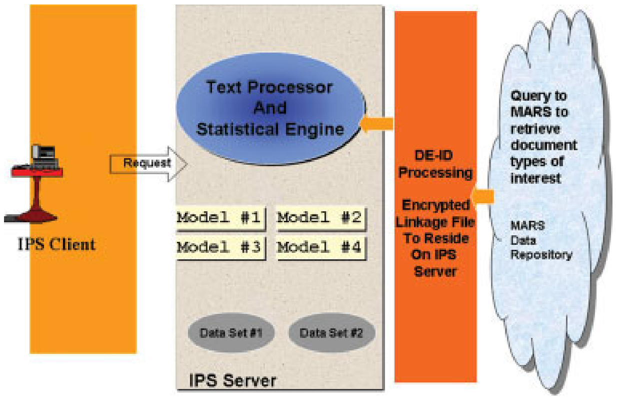
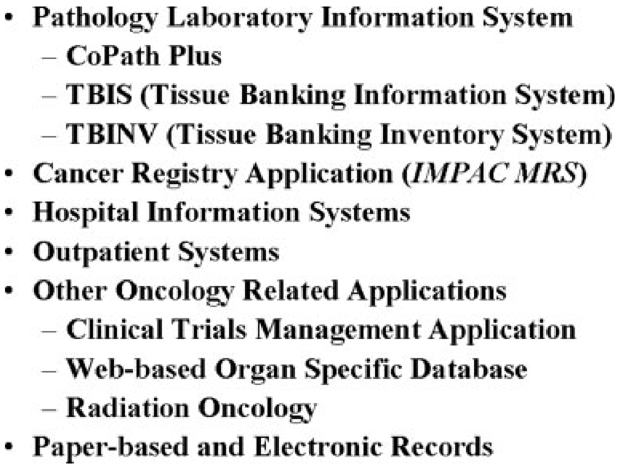


**FIGURE 6.** This is a pictorial representation of the process of data request, structure of information generation, retrieval, storage, and encryption. IPS indicates intrusion protection system; DE-ID, deidentification software engine; MARS, Medical Archival System.



- Pathology Laboratory Information System
  - CoPath Plus
  - TBIS (Tissue Banking Information System)
  - TBINV (Tissue Banking Inventory System)
- Cancer Registry Application (*IMPAC MRS*)
- Hospital Information Systems
- Outpatient Systems
- Other Oncology Related Applications
  - Clinical Trials Management Application
  - Web-based Organ Specific Database
  - Radiation Oncology
- Paper-based and Electronic Records

**FIGURE 7.** This is a list of some critical data sources used by the Honest Broker Facility. These data sources are part of affiliated facilities and are accessible to the Honest Broker Facility. IMPAC MRS indicates the IMPAC Medical Registry Services software system.

and the data managers for Medical Oncology and Radiation Oncology.

### Oversight for Tissue and Biologic Specimen Disbursement

Oversight for tissue and biologic specimen disbursement is provided by a number of organ-specific Tissue Utilization Committees (TUCs). These committees are within the University of Pittsburgh's translational and clinical programs. The University of Pittsburgh has functioning TUCs in the following organ sites: lung, head and neck, genitourinary, gastrointestinal, women's health, melanoma, liver and transplantation, and non-neoplastic lung diseases.

The committee provides representation to the different groups involved in decision making and research specimen usage for that particular organ type (surgery, oncology, pathology, researchers). Each of these committees makes binding recommendations to the personnel of the Tissue Bank for the priorities for distribution of tissue and biologic materials. There is an Institutional Oversight Committee that oversees the different organ-specific TUCs and serves as a final arbitrator in case of conflicts that are not resolved in the organ-specific TUC. The oversight committee consists of clinical and research leaders at the University of Pittsburgh. The oversight committee also serves the role of an internal scientific advisory board.

### Mechanisms for Prioritization of Biologic Specimens

The prioritization protocol is consistent with institutional policies. However, there are variations from organ system to organ system, depending on the different projects. The criteria for prioritization are: 1) Specialized Programs of Research Excellence (SPORE) projects; 2) exploratory pilot projects directed at SPORE project development; 3) projects funded by federally funded, peer-reviewed agencies; 4) projects funded by nonfederal agencies; and 5) projects funded by industry. The TUCs do have the authority to make exceptions with the approval of the Institutional Oversight Committee.

## RESULTS

The Honest Broker Facility received IRB approval in May 2003 (available at: http://cancerregistrynetwork.upmc.com/research/HB/honestindex.html accessed on July 23, 2008). Four months were required for training personnel and accomplishing paperwork for the certification of honest brokers. The existence of the system was announced to the staff and faculty of the University of Pittsburgh in October 2003.

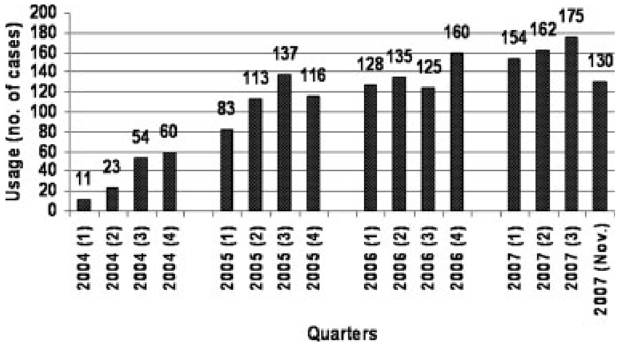


**FIGURE 8.** This chart illustrates the quarterly volume of cases handled by the Honest Broker Facility from 2004 to November 2007.

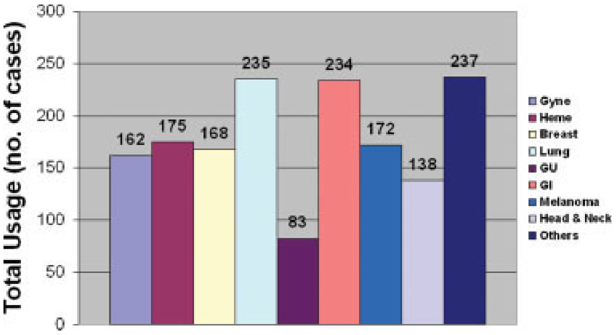


**FIGURE 9.** This chart shows the details of case volume handled by the Honest Broker Facility delineated by organ type. Gyne indicates gynecologic; Heme, hematologic; GU, genitourinary; GI, gastrointestinal.

The initial response to the facility was slow, and the last 3 months of 2003 generated only 6 requests for the Honest Broker Facility. The volume of research requests increased significantly in 2004. The calendar year 2004 generated 148 requests. The calendar year 2005 generated 449 requests. The calendar year 2006 generated 548 requests. The first 11 months of calendar year 2007 have generated 621 requests. The volume of requests is shown in Figure 8.

Requests for the Honest Broker Facility have come from all major oncology areas. The Honest Broker Facility has handled requests from all of the major organ type groups. These include the Pulmonary Group, the Head and Neck Group, the Gastrointestinal Diseases Group, the Genitourinary and Prostate Group, the Hematology Group, the Skin and Melanoma Group, and the Gynecology Diseases Group, including the Breast Group. The volume of requests from the different organ types since the inception of the Honest Broker Facility is shown in Figure 9. It should be noted the Breast and Gynecologic Oncology Group started using the facility in January 2006.

The Honest Broker Facility has received work requests for a variety of different tasks. These include preparatory for research, research projects, presentations and abstracts, quality and process improvement, assessment of incidence of disease, and marketing of clinical programs as well as for patient safety initiatives, clinical quality control, and quality improvement. We evaluated these requests to assess distribution by organ type. The detailed breakup of these requests is shown in Figure 10.

How does an investigator use the Honest Broker Facility? A researcher can approach any of the constituents of the Honest Broker Facility with a research request. The research request can be for tissue, biologic specimens, or clinical data. This specific component of the Honest Broker Facility approached by the investigator evaluates the research requests and identifies the different components of the Honest Broker Facility that would play a role in fulfilling the request. One of the constituent facilities is designated as the primary handler of the requests. This facility interacts with the other components involved in the request. This primary facility communicates with the researcher, ensures that all of the requested tissue/biologic specimens have been retrieved, and collates the data. The entire set of tissue and biologic specimens and annotating data is deidentified and then provided to the investigator.

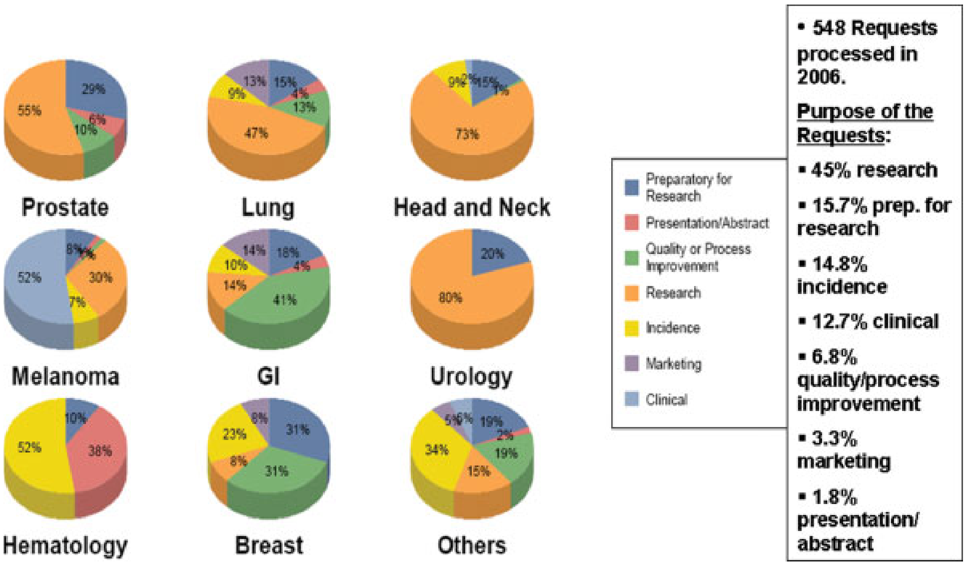
This honest broker system has been used by entities other than the University of Pittsburgh. A similar model has been applied by the Cooperative Prostate Cancer Tissue Resource[3,20,21] and by the Pennsylvania Cancer Alliance Bioinformatics Consortium. In addition, similar protocols were adopted for case retrieval for the Shared Pathology Informatics Network validation studies.[22]

## DISCUSSION

The Honest Broker Facility is now a well established mechanism for deidentified tissue and data disbursement. The facility has become very popular in a short time. This is borne by the incremental increase in the use of the facility over the last 4 years. The popularity of the Honest Broker Facility has started creating logistic issues, especially pertaining to staffing and turnaround. There are certain aspects of the Honest Broker Facility that need to be considered when creating a facility similar to that at the University of Pittsburgh.

### Training Honest Brokers

Training is an important aspect of maintaining uniform functionality of the Honest Broker Facility. The facility has seen a significant increase in honest brokers over the last 4 years. The Honest Broker Facility started with 5 honest brokers and now has 33 honest brokers. The initial aspect of training focuses on explaining the com-



- **548 Requests processed in 2006.**

**Purpose of the Requests:**

- **45% research**
- **15.7% prep. for research**
- **14.8% incidence**
- **12.7% clinical**
- **6.8% quality/process improvement**
- **3.3% marketing**
- **1.8% presentation/ abstract**

**FIGURE 10.** These pie charts detail the many different reasons for requesting honest broker services by researchers focused on the various organ systems. GI indicates gastrointestinal; prep, preparation.

pliance guidelines and objectives of the Honest Broker Facility, discussing the philosophy of existence of the facility, and completion of the IRB-mandated research models. These steps provide the new honest brokers with conceptual details of the Honest Broker Facility. Then, the honest brokers are trained on the software available for extracting data. This includes the honest broker tracking tool as well as mechanisms for deidentification.

## Specialization of Cancer Registrars

Another important parallel initiative has focused on creating a pool of specialized cancer registrars who work in cancer programs that are based on specific organ systems. These registrars are involved in collecting information on patients with a specific cancer. The information collected consists of the state-mandated reporting requirements from the Cancer Registry. In addition, these ‘specialized’ cancer registrars collect additional data elements for research purposes that have been approved by the IRB of the University of Pittsburgh. These cancer registrars also frequently approach the clinical caregivers to resolve data discrepancies among different sources.

Thus, these cancer registrars focus in on a cancer program for a particular organ system. Their work could be considered representative; however, this specialized approach serves to increase their knowledge base and awareness of issues related to a particular subset of tissues and tumor types. These registrars perform data entry for the state-mandated clinical function of the Cancer Registry. In addition, they handle specific requests for their area of concentration. This ensures a higher quality of data entry and retrieval.

In addition to increasing the clinical and translational research skills of the specialized cancer registrars, they become experts in a variety of clinical information systems from which they extract phenotypic data. They also develop a variety of informatics skills in the areas of data processing, data deidentification, and the use data warehouses. In particular, they have developed skills in data mining tools using both commercial tools and their own customized algorithms for clinical and translational research.

## Increased Availability of Tissue/Data to Investigators

Numerous annotated tissue repositories already exist in this institution and its affiliated cancer center. These include frozen as well as paraffin-embedded tissue materials and other biologic materials. The overall objective is to make them available to a wider research community in a manner that is efficient, rapid, and compliant with legal and ethical concerns. There is significant awareness locally regarding the benefits of expanding use of our resources in collaborative projects. The creation of an institutional tissue resource as well as an institutional Honest Broker Facility has served to accelerate access to tissue, biologic materials, and annotating data. Furthermore, many tissue bank-focused projects do not take into account the vast resources of paraffin archives housed in many academic pathology departments[2,14] that are available for use. This initiative will serve to bring down barriers at the institutional level and provide access to all forms of biologic materials and data.

The structure and design of the University of Pittsburgh honest broker system has been presented at a meeting of the International Society for Biological and Environmental Repositories. It also has been shared with many collaborating academic institutions.

## Funding

The initial provision of adequate resources is required to ensure the success of this institutional facility. There has been upfront investment by the institution in terms of personnel. The Honest Broker Facility also has been incorporated into grant submissions to provide committed funding for these activities. The principal investigator who submits a grant proposal acts as a consultant to the Honest Broker Facility. The broad outline of the project is discussed in the proposal, and an estimate is made of the amount of time needed to fulfill projected needs of the project. The principal investigator then incorporates the anticipated personnel requirements into the budget of the proposal. The facility also functions on a fee-for-service basis. The fee-for-service mechanism applies to work done on nongrant-funded initiatives. Fees for services are based on an hourly rate for providing honest broker/deidentification services, data accrual, database creation, and chart review. These different monetary mechanisms have helped provide resources for the facility to survive and grow.

The creation of an institutional Honest Broker Facility has created a robust mechanism for data accrual and disbursement. In addition, it has led to the development of a significant informatics infrastructure to support this facility's functions. This has decreased turnaround time for providing data associated with samples provided to investigators. We hope that this system will promote more robust, efficient, and clinically and biologically relevant studies of biomarkers. Studies resulting from the creation of this facility may allow for better classification of cancer types, more accurate assessment of disease prognosis, a better ability to identify the most appropriate individuals for clinical trial participation, and better surrogate markers of disease progression and/or response to therapy. The biomedical informatics infrastructure and the honest broker tools created to serve the Honest Broker Facility also will be made available for use by outside institutions. We hoped that this approach focused on sharing our experience and software tools will benefit research on a more global scale.

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