

The NIAID Division of AIDS enterprise information system: integrated decision support for global clinical research programs

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ABSTRACT

The National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS) Enterprise Information System (DAIDS-ES) is a web-based system that supports NIAID in the scientific, strategic, and tactical management of its global clinical research programs for HIV/AIDS vaccines, prevention, and therapeutics. Different from most commercial clinical trials information systems, which are typically protocol-driven, the DAIDS-ES was built to exchange information with those types of systems and integrate it in ways that help scientific program directors lead the research effort and keep pace with the complex and ever-changing global HIV/AIDS pandemic. Whereas commercially available clinical trials support systems are not usually disease-focused, DAIDS-ES was specifically designed to capture and incorporate unique scientific, demographic, and logistical aspects of HIV/AIDS treatment, prevention, and vaccine research in order to provide a rich source of information to guide informed decision-making. Sharing data across its internal components and with external systems, using defined vocabularies, open standards and flexible interfaces, the DAIDS-ES enables NIAID, its global collaborators and stakeholders, access to timely, quality information about NIAID-supported clinical trials which is utilized to: (1) analyze the research portfolio, assess capacity, identify opportunities, and avoid redundancies; (2) help support study safety, quality, ethics, and regulatory compliance; (3) conduct evidence-based policy analysis and business process re-engineering for improved efficiency. This report summarizes how the DAIDS-ES was conceptualized, how it differs from typical clinical trial support systems, the rationale for key design choices, and examples of how it is being used to advance the efficiency and effectiveness of NIAID's HIV/AIDS clinical research programs.

INTRODUCTION

The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), US Department of Health and Human Services, conducts and supports basic and applied research to understand, treat, and prevent infectious, immunologic, and allergic diseases. In 1986, NIAID began an evolving group of global clinical trials networks linking hundreds of institutions and thousands of collaborators to test new interventions for HIV/AIDS.¹ Yet, despite advances, the epidemic expanded unabated, especially in the developing world. The period 1997–2002 witnessed the annual global

AIDS deaths toll reach 2 million, with nearly 7000 new infections daily.² In response, NIAID doubled its trial portfolio and extended its capacity, adding sites in more than 30 countries. After the NIH budget doubling (2003), with the prospect of protracted fiscal constraints, in 2006 NIAID restructured its HIV/AIDS clinical trial networks for greater flexibility and efficiency.³ As part of this effort, the DAIDS-ES was developed to enhance decision support for the scientific management of these complex programs. This article highlights the objectives and design choices made in developing this unique clinical research support system designed to assist NIAID in its scientific leadership role, sponsoring and guiding the world's largest clinical trials programs for HIV/AIDS.

CASE DESCRIPTION

Commercially available clinical trials information systems are designed primarily for use in manufacturer-sponsored trials seeking to evaluate the safety and efficacy of specific products. NIAID, by contrast, has a public health orientation and a goal to understand disease pathogenesis through hypothesis-driven research. Managing this kind of trials program requires a different type of information support that can provide the ability to look across hundreds of trials, products, investigators, and institutions. By 2003, the rapid growth of NIAID's HIV/AIDS programs had produced a situation in which research managers could not accurately or efficiently assess the trials portfolio, monitor progress, track capacity, respond to data calls, or review policies and business processes. Queries of protocols by study agent (or class), frequency/types of serious adverse events, or site performance took excessive amounts of time because of the need to specify, locate, and amalgamate data from multiple disparate, incompatible databases and systems, maintained by organizations over which NIAID had little control. In order to effectively carry out its dual roles as scientific leaders and sponsors of clinical research, NIAID required an information system capable of providing both high-level and detailed views of data stored in multiple different clinical trial management and support systems (including safety, regulatory, laboratory and pharmacy databases, site monitoring/quality assurance programs, trials sites and operations centers). This report describes the rationale and approach by which NIAID developed the DAIDS-ES, tailored to its research leadership mission.

Case report

METHODS OF IMPLEMENTATION

The DAIDS-ES was designed to exchange data with multiple collaborator systems, and integrate it within and across six core functional components:

1. A centralized database of clinical studies
2. A central registry of people and organizations and their study-specific roles
3. An online serious adverse experience reporting system
4. A clinical site-monitoring (quality assurance) database
5. An online protocol registration system
6. An investigational new drug database to manage regulatory submissions and files

A schematic representation of the DAIDS-ES logical architecture is shown in figure 1.

Because of its reliance on information from collaborator data stores, some of the most critical design decisions for the DAIDS-ES were around standards for data exchange and transfer, terminology and vocabulary, and data analysis. Five criteria were invoked in selecting standards: (1) environment—standards acceptability across more than 20 collaborators; (2) technology—the extent to which the technologies of NIAID and its collaborators could accommodate the standards; (3) implementation—the effort required to apply the standards within the DAIDS-ES and collaborator systems' design and business logic; (4) cost—the fees required to utilize the standards; (5) future requirements—the potential for mapping and reuse, alignment and data exchange with other external systems in the future.

As an example, the selection of a standardized dictionary for study agents (eg, drugs, vaccines) was driven by requirements to provide the ability not only to identify studies that involve specific agents, but also to locate studies by regimens (eg, involving particular drug classes), to map generic and brand names to the same dictionary term, to support synonym-based searches, and to provide the ability to link drugs to their respective manufacturers. Table 1 shows a comparison of four drug dictionary standards and the aspects of one of them, medical subject headings (MeSH),⁴ that made it best suited, namely: (1) inclusion of many products used in DAIDS studies; (2) frequent updating; (3) available at no cost; (4) easily accessible. In addition, US Public Law 110-85 (FDAAA) requires submission of data to NLM's (National Library of Medicine) Clinical Trials.gov, for which automated submissions require MeSH coding for study products.

Detailed descriptions of each functional component, the system technical architecture, and other design features (eg, technology stack, other data standards, data access, and interchange specifications) are provided in the online appendix. The system was deployed in August 2006, initially providing two user functions, serving approximately 250 NIAID users. Since that time, four additional user functions were added/upgraded as components of 11 releases, and access expanded to nearly 3500 of NIAID's global clinical trials' investigators and collaborators. In 2010, the DAIDS-ES generated approximately 40 000 web service calls and processed over a quarter of a million interactions across its core components.

EXAMPLES AND OBSERVATIONS

Three illustrative examples demonstrate some of the ways in which the DAIDS-ES supports the scientific mission of NIAID.

Portfolio analysis and capacity assessment

NIAID requires accurate, timely information about the status of hundreds of ongoing and planned studies. New insights into the biology of HIV disease are rapidly emerging, resulting in novel hypotheses and agents to test. To identify opportunities and avoid redundancies, NIAID must assess the breadth of its portfolio, identify gaps, determine capacity, and monitor resource allocations. As shown in figure 2, the DAIDS-ES supports portfolio analysis, integrating data on intervention types, participant demographics, country-specific accruals, and protocol status, across hundreds of studies, sites, collaborative groups, and study populations, thereby providing NIAID a detailed view of the AIDS clinical research investment, which can be used to inform decision-making, monitor progress, track capacity, and respond to data calls.

Study concept evaluation and business process analysis

Each year NIAID's DAIDS receives hundreds of ideas proposing studies to test new interventions for HIV/AIDS. In addition to outside peer review, concepts undergo rigorous evaluation within DAIDS by medical/scientific, safety, regulatory, and ethical experts, to ensure the highest standards of clinical research, and alignment with research priorities. The efficiency of this review process can be monitored using DAIDS-ES data. As shown in table 2, the time elapsed from concept receipt to review, and the interval between review and transmittal of

Figure 1 A graphic depiction of the logical architecture of the DAIDS-ES showing architectural elements. Enterprise Foundation—the logical data store into which collaborator data flow. DAIDS-ES components—the user functions that support one or more DAIDS business areas. DAIDS Portal—a web-based dashboard providing a view into the different core features and data associated with each DAIDS business area. IND, investigational new drug.

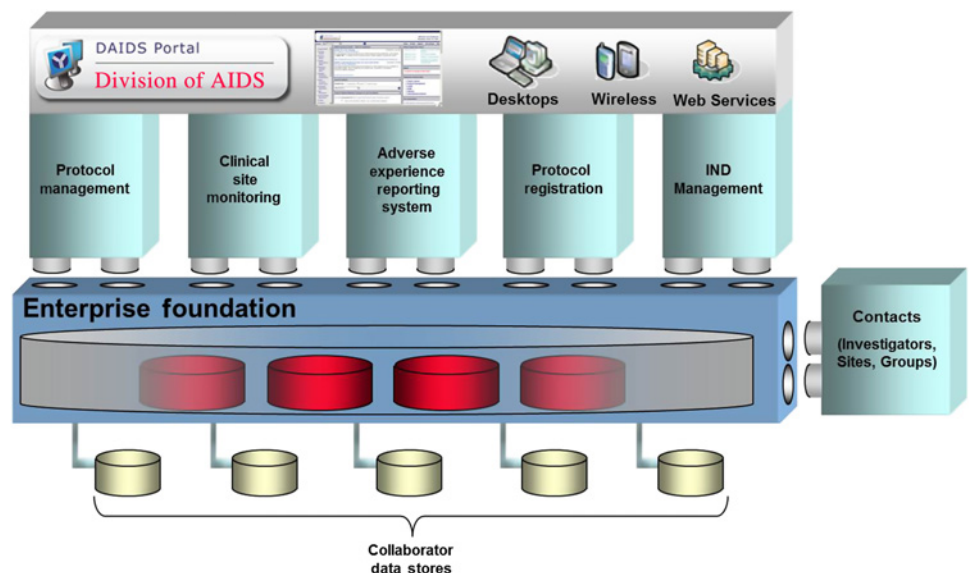


Table 1 DAIDS-ES drug dictionary comparison (2006)

Dictionary	Number of DAIDS-ES study agents for which coding was available	Number of study agents for which codes were not available	Total number of study agents	Dictionary-specific features	Dictionary update frequency	Format	Initial cost	Access
Medical subject headings (MeSH) ⁴	131	46	177	Unique code and drug class available for each product; of 46 not available, 35 are vaccines or vaccine components; generic brand names map to a unique code (GPI) for each product	Weekly/yearly	XML	No cost	Internet-browsable dictionary
Master drug database (MDDb) ⁵	74	103	177	Includes a generic product identifier	Daily/monthly	ASCII	US\$18000	CD
National drug code directory (NDC) ⁶	74	103	177	Multiple codes for same product exists for different manufacturer; no unique code for generics; codes change based on manufacturer, dosage form and strength; many non-US drugs not included	Quarterly	ASCII	No cost	Internet-browsable dictionary
AHFS pharmacologic-therapeutic classification system ⁷	80	97	177	Codes available only for drug classes, not specific drugs; no download files available	6 months/1 year	None	US\$100–200	PC/PDA application

Data in this table was obtained in 2006.

feedback to the investigator, can be compared with each process's target time, with one another, and with the total process time. Presently, data indicate that, on average, these reviews take place within their target time allowances and often more quickly, suggesting that even faster turnaround times may be achievable. More detailed 'looks' at other elements of the protocol lifecycle are currently underway with the aim to understand how the time to complete clinical trials can be shortened.

Study quality management and policy analysis

DAIDS-ES was designed to help NIAID improve efficiency in clinical research through evidence-based policy analysis. An example can be found in the area of clinical study monitoring, a costly component of clinical trials quality assurance. In one NIAID program, policy prescribes that before the arrival of study monitors, trial sites are provided advance notice of patient identification numbers (PIDs) for half of the participant charts selected for review ('announced' PIDs), with the remainder presented upon arrival. The thought behind this policy is that advance notification of PIDs enables sites to correct mistakes or alter contents of participants' charts, whereas withholding PIDs until monitor arrival can prevent this (for half the charts). Unfortunately, a problem resultant from this policy is that, upon arrival of the monitors and disclosure of the previously 'unannounced' PIDs, site staff are often unable to obtain the designated charts (ie, they may be in a remote location), therefore monitors are unable to meet specified protocol risk-based monitoring targets. Data from the DAIDS-ES supported a preliminary analysis to determine if there was any difference in the number of findings (eg, protocol deviations) monitors observed when reviewing announced versus unannounced charts. Figure 3 shows that, for 11 of the 19 sites studied, monitors actually reported greater numbers of findings in the announced charts. While these results are preliminary and there is likely no statistically significant difference between groups, the initial indication is that sites do not alter or make corrections to announced charts, and therefore the presumptive basis for the policy may be unfounded. If verified in further studies, a policy change (wherein all PIDs were announced in advance) could increase monitoring efficiency by assuring that participant charts are available, and designated risk-based quality assurance goals could more consistently be achieved.

DISCUSSION

The DAIDS-ES was designed to diminish information gaps as barriers to AIDS clinical research by: (1) easing access to information, saving time, and diminishing backlogs; (2) repurposing data for efficiency, accuracy, and cost avoidance; (3) improving business processes and policies for greater efficiency. Without baseline performance measures and costs for analysis, we cannot yet quantify returns-on-investment for the DAIDS-ES; however, early qualitative assessments indicate that the system is making progress toward its design objectives (see online appendix). With the costs of clinical data interchange in the biopharmaceutical industry running upwards of a billion dollars annually,⁸ it is difficult to imagine that greater utilization of systems providing common vocabularies and data standards will not be shown to save substantial resources.

Three additional intended benefits of the DAIDS-ES are worth mentioning: (1) risk reduction; (2) increased flexibility; (3) data mining for new opportunities. NIAID's HIV/AIDS clinical trials programs are supported through competitive award mechanisms, with funding periods typically ranging from 4 to 7 years.

Case report

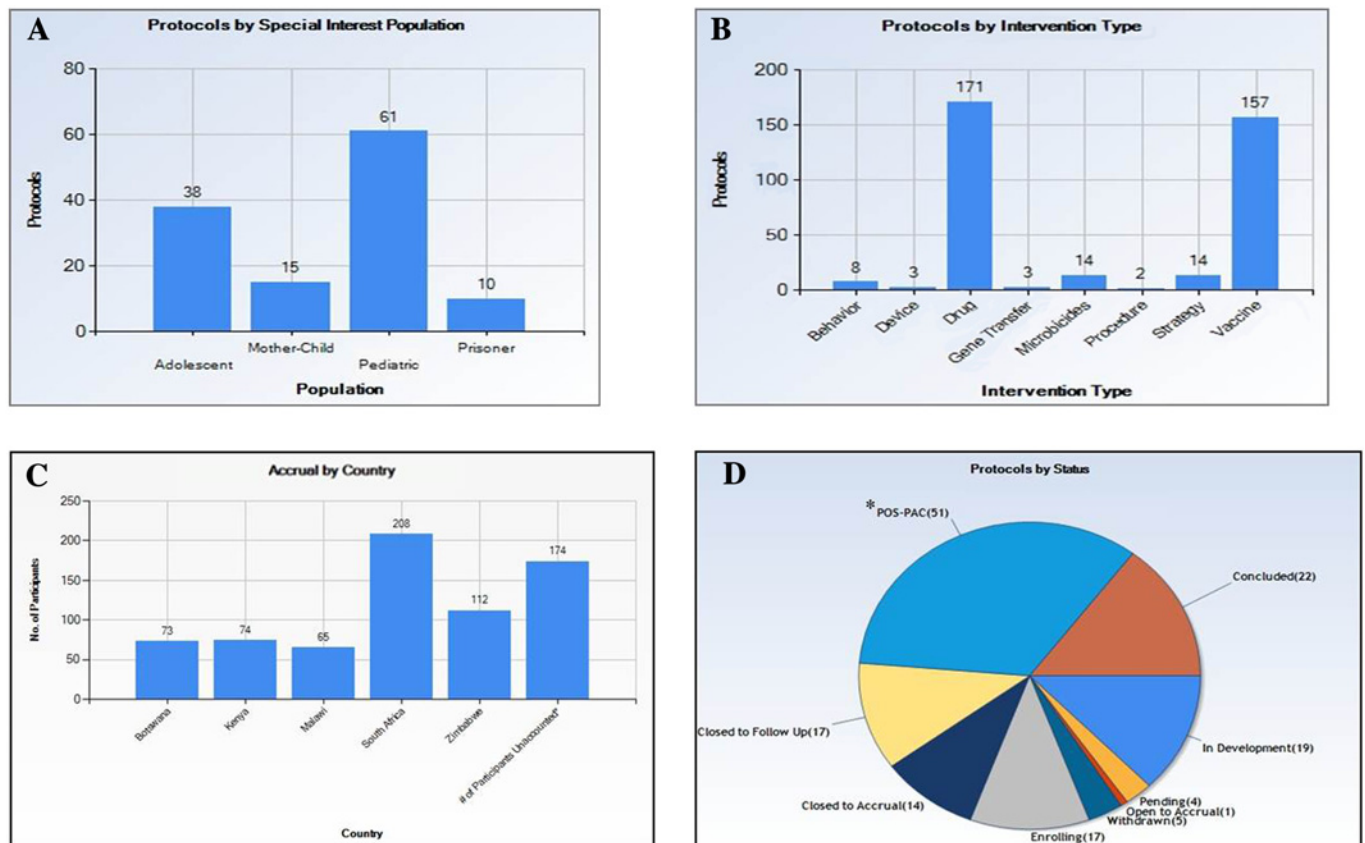


Figure 2 Four sample views of clinical trial portfolio analyses from the DAIDS-ES. (A) Protocols by special interest population (participants). (B) Protocols by intervention type (eight types shown). (C) Accrual by country. (D) Protocols by status (actual number). POS-PAC, participants off study—primary analysis complete.

With new studies continuously being implemented (and large trials often taking 3–5 years), competitive renewals take place in the midst of ongoing trials, often resulting in changes to research collaborators and transitions, which can limit capacity because of data loss, corruption, or incompatibility. The DAIDS-ES should help reduce these risks because information formerly stored only in collaborator-based systems now resides in a central NIAID-hosted database. With control over its data standards, NIAID should be in a better position to assure that future IT investments are designed for maximal utility, flexibility, and data reuse. Finally, in the area of emerging and re-emerging infectious diseases, new threats to public health can arise rapidly (eg, MRSA, XTR-TB, novel H1N1 influenza, SARS); as such, tools such as the DAIDS-ES may help investigators and policy-makers to identify opportunities and act expeditiously in safeguarding public health.

Table 2 Clinical trial concept review processing times

	Time from concept receipt to review (A)	Time from concept review to investigator feedback (B)	Total concept review process time (A+B)
Process target	21	14	35
Median (actual)	13	13	27
Median difference*	–8	–1	–8
No of reviews	106	106	106

Data presented in calendar days.

*Median of actual time minus target time for the process.

Lastly, although the system driver was to create a solution for managing the NIAID HIV/AIDS clinical trials programs, the DAIDS-ES was designed to flexibly and robustly represent and integrate clinical research information in the larger environment of an extramural NIH program. Since the vast majority of NIH-supported clinical research is conducted extramurally, through

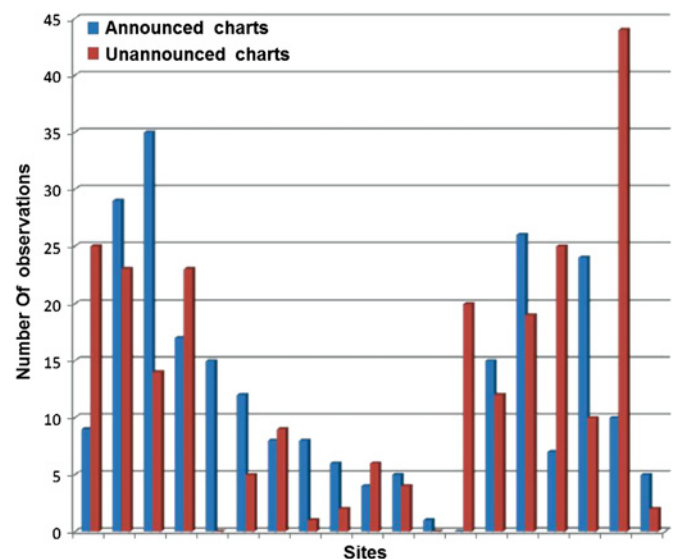


Figure 3 Monitoring observations in announced versus unannounced charts. Numbers of observations made by on-site monitors reviewing announced versus unannounced charts at the same clinical trial sites.

programs operating under the same overarching fiscal and regulatory authorities and policies, the DAIDS-ES offers substantial reuse potential within NIAID and other NIH Institutes and Centers. Outside of NIH, patient/disease advocacy organizations may also find use for the DAIDS-ES (or components) in overseeing and guiding their clinical research investments.

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Data sharing statement In NIH's view, all data should be considered for data sharing. Data should be made as widely and freely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data.

REFERENCES

1. **Kagan JM**, Kane M, Quinlan KM, *et al*. Developing a conceptual framework for an evaluation system for the NIAID HIV/AIDS clinical trials networks. *Health Res Policy Syst* 2009;**7**:12.
2. **UNAIDS**. *UNAIDS AIDS epidemic update 2009*. 2009. <http://www.unaids.org/en/dataanalysis/epidemiology/2009aidsepidemicupdate/> (accessed 18 May 2011).
3. <http://www.niaid.nih.gov/news/newsreleases/2006/Pages/leadership.aspx> (accessed 18 May 2011).
4. **U.S. National Library of Medicine**. *Medical Subject Headings (MeSH)*. <http://www.nlm.nih.gov/mesh/meshhome.html> (accessed 18 May 2011).
5. **Wolters Kluwer Health**. *Master Drug Data Base v2.5 (MDDB®)*. 2011. <http://www.medspan.com/master-drug-database.aspx> (accessed 18 May 2011).
6. **U.S. Food & Drug Administration**. *National Drug Code Directory*. 2011. <http://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm> (accessed 18 May 2011).
7. **American Society of Health-System Pharmacists**. *AHFS Pharmacologic-Therapeutic Classification System*. 2011. <http://www.ahfsdruginformation.com/class/index.aspx> (accessed 18 May 2011).
8. **Kush RD**. *The Cost of Clinical Data Interchange in Clinical Trials*. 2001. http://www.cdisc.org/stuff/contentmgr/files/0/5918b70f2479b34d2753ad88d23d2b1d/misc/cost_of_cdi_in_ct.pdf (accessed 18 May 2011).
9. **McCray AT**. Better access to information about clinical trials. *Ann Intern Med* 2000;**133**:609–14.



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