HERC
Health Economics Resource Center

January 25, 2000

VA Health Economics Resource Center Technical Report #2

Human Subjects Compliance Programs: Optimal Operating Costs in VA

Todd H. Wagner, PhD
Paul G. Barnett, PhD

Dedicated to improving the quality of health economics research

EXECUTIVE SUMMARY

This report estimates the optimal costs for operating a human subjects compliance program.

Optimal Institutional Review Board (IRB) organization

- The major cost category in operating a human subjects compliance program is personnel.
- According to expert opinion, a human subjects professional staff employee can be expected to review 300-350 protocols per year**.**
- To complete reviews in a timely manner, institutions adjust the frequency with which the committees meet and the number of committees. Medium volume institutions typically have 1-2 committees, whereas high volume IRBs have between 3 and 5 committees.

RDIS information

- A total of 129 VA medical centers conducted research with human subjects in 1998. Among those sites conducting human subjects research, the average number of studies was 123.
- A large proportion of VA studies with human subjects was not directly funded by additional research allocations. According to the VA Research and Development Information System (RDIS), approximately 63% of the studies had no additional allocated funds in that calendar year. Nevertheless, these unfunded studies may incur IRB costs.
- Forty-three medical centers (33%) conducted 20 or fewer studies; 23 centers (18%) conducted 5 or fewer studies. If these organizations operate their own IRB, there would be potential efficiency and quality problems.

Projected optimal costs to operate an IRB in the VA

- Personnel costs are the major cost of operating compliance programs. For a medium volume and a high volume VA, personnel costs represent 86.6% and

85.7% of the projected costs, respectively.

- For the medium volume VA, the projected optimal staff includes a Ph.D.-level director, one FTE administrative assistant, one FTE computer analyst and 12 FTE professional staff. The IRB chair, assumed to be a physician, was allotted a 0.5 FTE and committee members were assigned 0.05 FTE. The total projected cost of operating compliance programs is $584,134 (22.3% of direct costs). The cost per protocol is approximately $1,578.
- For the large volume VA, the projected optimal staff includes 5 FTE staff employees, one FTE Ph.D.-level director, one FTE administrative assistant, and one FTE computer data analyst. The IRB chair, assumed to be a physician, was allocated a 0.5 FTE and committee members were assigned 0.05 FTE. The total cost of operating a compliance program in a large VA medical center is $1,009,760 (8.8% of direct costs). The cost per protocol is approximately $730.

Reasons for scale economies

- According to a recent study, high volume IRBs spend about half the time reviewing a protocol that is spent by medium volume IRBs. Although this may be related to quality differences, large volume IRBs may also be more efficient. Through repetition, high volume IRBs may be able to refine their operation, in a sense following the maxim, "practice makes perfect."

Study limitations

- Whether or not there are greater efficiencies in the larger institutions or the extent to which quality is related to cost is beyond the scope of this analysis.
- An optimally staffed and funded IRB does not guarantee high-quality reviews. Additional research is necessary to understand what factors are related to quality and how quality relates to cost.
- Capital costs are not included in our estimates. For non-VA sites, one would need to add capital costs; this would increase the total cost estimates and the cost per protocol by approximately 5%.

Human subjects compliance programs

1. Specific Aims

1) To determine the recommended staffing, support personnel and the number of Institutional Review Board (IRB) panel members needed to review the number of human subjects protocols considered by an average volume VA medical center.
2) To use the Research and Development Information System (RDIS) to compare VA medical centers by research revenues and types of studies.
3) To use information from Aims 1 and 2 to project IRB operating costs for a hypothetical optimally staffed large and medium volume VA medical center.

2. Methods

To address the specific aims, we followed three consecutive steps. First, through open-ended interviews with human subjects experts, we obtained information on the *optimal* allocation of professional staff and reimbursement for panel members. We also discussed with these experts how IRBs have changed in past years and their anticipated changes in the years to come.

Second, to compare VA medical centers by research revenues and type of fiscal support, we obtained data from the Research and Development Information System (RDIS). The information was from the 1998 fiscal year and was aggregated for each medical center. For each medical center we obtained the number of studies involving human subjects. Medical centers were ranked according to the number of studies in each category. We then separated the ranked list into tertiles and reported on the average for the high and medium volume medical centers.

Lastly, using information from our expert interviews, data from a recent OPRR report, and data from RDIS, we estimated the costs of operating an optimally configured human subjects program in a medium and high volume VA. Volume was based on the number of human subjects studies conducted in 1998 (FY).

It should be noted that many institutions conduct research with biohazards, animals, and

radioisotopes. This report does not cover compliance programs for biohazards or animal subjects.

3. Results

3.1. Expert recommendations

We interviewed three human subjects experts. One of these persons directs human subjects at a major non-profit research organization and the other two direct human subjects at medical schools in well-known academic institutions. One of these persons is also the current president of Applied Research Ethics National Association (ARENA), which is the professional organization for human subjects professionals.

Background on compliance programs

Investigators conducting human subjects research must first obtain approval before the study can begin. For this, the application and research protocol are submitted to the IRB. Most research organizations have their own IRB or are affiliated with institutions that have IRBs. In some cases, the IRB is handled through a private company for a set fee.

Once the application is received, the IRB conducts an internal review to ensure completeness. The application material is then passed to a review committee. Although the background of the committee members is very diverse, sometimes consultants are enlisted to review the protocol. Use of consultants varies widely from institution to institution.

Although federal regulation sets the foundation for how IRBs operate, most IRBs have evolved independently. Consequently, while most IRBs meet federal regulations, they "look" and operate in very different manners. To understand this variation, OPRR recently contracted with James Bell and Associates to survey all institutions that had multiple project assurances (MPA).[1] This study, hereafter known as the Bell Report, updated an earlier study done in 1978 by Gray and colleagues.[2]

At typical institutions, committees convene monthly or bimonthly to review protocols. In

each session, the committee reviews approximately 8-16 initial protocols, of which 2-4 are full, 3-6 are exempted, and 3-6 are expedited. In the session, 1-3 amended and 2-4 reapproval applications are also reviewed. Bell and Associates found that an IRB committee at a typical high-volume facility can review 22 protocols in a session (4 full, 6 exempted, 6 expedited, 4 continuing and 3 amended), whereas an IRB committee at a medium volume facility usually spends more time on each protocol, reviewing 11 protocols in the same time (2 full, 3 exempted, 3 expedited, 2 continuing and 1 amended). These numbers vary dramatically depending on the complexity of the protocols and the committee=s experience. Committee meetings usually last 2-3 hours.

On cost

In assessing the administrative costs of operating human subjects compliance programs, the following are the major cost categories:

- Personnel
- Space
- Computers, databases, equipment and supplies
- Training and education

Personnel costs are the primary cost driver. Although the key informants did not know of any research identifying the optimal number protocols to be reviewed by a full-time equivalent (FTE) employee, each believed that an optimal professional staff would be one FTE per 300-350 protocols. This translates into a workload of reviewing one to two protocols per day, which the experts agreed was manageable in conjunction with the staff=s other responsibilities, such as holding training sessions for researchers, developing standard operating procedures, etc.

While personnel represent the largest cost category, training and education are also costly. Personnel are sent to national meetings and attend training sessions. Training costs can total $75,000 to $100,000 per year.

In addition, the cost of renting space (or property financing) can be significant. Because

these costs are handled very differently in the VA system, these costs are not included in our total. To make our estimates comparable to non-VA sites, one would need to add these costs; this would increase the total cost estimates and the cost per protocol by approximately 5%.

On quality

Within an assurance office, quality is related to two necessary factors: (1) the protocol reviewer=s training and experience and (2) time for reviewing each protocol. Alone, neither factor is sufficient to ensure high quality. The experts agreed that more needs to be done to train professional staff, to set national quality standards, and to reimburse committee members for their time.

Institutions may also have differing levels of quality depending on the volume of their work. Organizations may experience quality problems if there is insufficient time to review each protocol. Alternatively, a human subjects committee that reviews too few protocols tend to be inefficient and of lower quality. This is because the committee cannot develop a "rhythm" and hone their standard operating procedures. No institutional knowledge is developed or retained. Experts suggest that facilities that review fewer than 100 protocols a year may suffer from this problem.

3.2. Ongoing research within the VA: a look at RDIS

To estimate the costs necessary to operate a human subjects compliance program at a medium and high volume VA facility, it is necessary to understand more about the research conducted at VA medical centers. Of all VA medical centers in FY 1998, 129 were conducting research projects involving human subjects. A total of 15,918 studies were conducted, with the greatest number of projects at West Los Angeles (n=762). The average number of studies among those sites conducting human subjects research was 123. However, a third of the sites (n=43) performed 20 or fewer studies and 23 (18%) carried out five or fewer studies.

Direct funding for these studies came from within the VA and from non-VA sources; the

amount of outside funding ranged considerably by medical center. For example, among the high-volume medical centers, West Los Angeles received a total of $20.2 million for human subjects research. Of this total, 88% was from non-VA sources, ranking West Los Angeles as first among high volume VA medical centers. For all medical centers, approximately 61% of all research dollars came from non-VA sources.

Interestingly, a large proportion of VA studies with human subjects were not directly funded by additional VA allocations or by grant revenues. According to RDIS, approximately 63% of all human subjects studies in the VA had no additional VA allocations or external grant funds in 1998. While many of these "unfounded" studies may have received research allocations in prior years, they incur present-day costs, including IRB costs.

3.3. Projected optimal costs

Information from experts and RDIS, which was reported in the previous two sections, was used to estimate the cost of operating a high-quality human subjects compliance program at a medium and a large VA medical center. In addition, we used data from the Bell Report,[1] which reported substantial information on IRB characteristics and effort expended.

The estimates for the medium volume VA were based on the average number of studies for all medical centers. The high volume estimates were based the average of the ten VA medical centers with the greatest number of research projects.

- The hypothetical medium volume VA had 123 human subjects studies, and we assumed that the IRB reviewed 370 protocols a year (our estimates for the ratio of studies to protocols are presented in the appendix).
- The hypothetical large volume VA had 461 human subjects studies, and we assumed that the IRB reviewed 1,383 protocols a year

Operating a human subjects compliance program requires personnel, office space, and supplies. As the number of protocols to review increases, so does the need for more personnel, space and supplies. We assumed that supplies include copying, office supplies, and phones,

varied directly with the number of protocols to review ($50 per protocol). However, the other inputs increase, but not at a linear rate. Personnel, for example, are usually hired full or part time. Whether or not their time is efficiently used depends on workload (i.e., the number of protocols to be reviewed) and other factors.

Institutions have a number of methods to ensure that the protocols are reviewed in a timely manner. Either the institution can add committees or it can have the committees meet more frequently. To standardize our cost estimates, we assumed that the committees met bimonthly and the only way to review more protocols was to add committees. All of the model parameters are listed in the technical appendix.

Medium volume VA: 370 protocols a year

For the medium volume VA, the *optimal* staffing would include a Ph.D.-level director, one FTE administrative assistant, a FTE computer analyst, and 12 FTE professional staff. The professional staff review each protocol before it goes to the committee. We also assumed that two committees review all protocols, meeting bimonthly. Each committee includes a chair and nine members. The IRB chair, assumed to be a physician, was allotted a 0.5 FTE and committee members were assigned 0.05 FTE. The total cost of operating an optimal compliance program is $584,134. This represents 22.3% of research revenues received. The cost per protocol is approximately $1,578. See Table 1 for the costs; a more detailed table of the costs is also included in the technical appendix.

Table 1: Projects costs for a typical medium and high volume VA medical center

	Volume	
	Medium	High
Number of projects in 1998 (RDIS)	123	461
Expected number of protocols per annum		
Initial		
full	81	302
exempted	21	77
expedited	36	133
Continuing	152	567
Amended	81	304
Subtotal	370	1,383
Optimal personnel allocation		
Director	1	1
Administrative Staff	1.5	5.0
Administrative Assistant	1	1
Computer analyst	1	1
Committee chairs	2	3.5
Committee members	18	32
Personnel costs		
Director	$ 93,750	$ 93,750
Administrative Staff	$ 90,000	$ 300,000
Administrative Assistant	$ 50,000	$ 50,000
Computer analyst	$ 75,000	$ 75,000
Committee chair(s)	$ 112,500	$ 196,875

Committee members	$ 84,375	$ 150,000
Consultants per initial full review	donated	donated
Subtotal	$ 505,625	$ 865,625
Operating costs*	$ 78,509	$ 144,135
Total IRB costs	$ 584,134	$ 1,009,760
Cost per review	$ 1,578	$ 730
Research revenues	$ 2,624,531	$11,486,620
IRB costs as percent of revenues	22.3%	8.8%

* Includes office supplies, computers, etc.

Large volume VA: 1,383 protocols a year

For an optimally configured large volume VA, operating the human subjects compliance programs required 5 FTE staff employees, a Ph.D.-level director, one FTE administrative assistant, and one FTE computer data analyst. See Table 1 for the costs; a more detailed table of the costs is also included in the technical appendix. We also estimated that it would take three human subjects committees meeting bimonthly, and a fourth committee meeting monthly to review the proposals. Each committee includes a chair and nine members. The IRB chair, assumed to be a physician, was allotted a 0.5 FTE and committee members were assigned 0.05 FTE. The cost of operating an optimal compliance program in a large VA medical center is $1,009,760. The cost per protocol is approximately $730. The cost of operating compliance programs for the high volume facility represents 8.8% of research revenues received by the medical center.

4. Conclusion

Operating a high-quality human subjects compliance program requires personnel that are well-trained and have sufficient time to review the protocols. In addition, the committee needs ample time to review the protocols. According to expert opinion, the optimal time required for a committee chair is 0.50 FTE and 0.05 FTE for the other committee members.

By following recommended staffing levels and by using data from the VA RDIS and data from the Bell Report, we estimated the cost of operating human subjects assurance programs. We found that a medium volume VA costs approximately $584,134 ($1,578 per protocol reviewed). The ten largest VA medical centers conduct four times more research than the average VA. The total cost of an assurance program in the high volume VA is considerably more, $1,009,760, but the cost per protocol reviewed ($730) is 54% less due to economies of scale.

It should be noted that these figures were estimated for the VA. Currently, the VA does not allocate funds for capital costs from its current operating budget. The cost of office space is thus excluded from our estimate. For non-VA sites, one would need to add capital costs; this would increase the total cost estimates and the cost per protocol by approximately 5%.

Outlook

The quality of human subjects review will likely increase in the next couple years as programs to train and accredit staff professionals become available. Such changes will be necessary, as research protocols are getting increasingly complex. Organizations that have been recently audited by the National Institutes of Health Office of Prevention from Research Risks (OPRR) will try to increase quality by hiring additional individuals and developing databases to track protocols. Other research institutions are likely to follow suit to avoid being audited.

Forty-eight (37%) VA medical centers have fewer than 34 studies; thus they are likely to review less than 100 protocols each year. To improve quality, it will be important for the VA to consider consolidating compliance programs in regional IRBs or "outsourcing" with other organizations. Outsourcing can be done (and is already being done) through the affiliated

academic medical center or private organizations.

This study raises a number of important issues that could be addressed with additional research. First, policy makers may wish to learn whether the VA is allocating the optimal funding for each medical center. Second, questions of whether or not there are greater efficiencies in the larger institutions would be a necessary step toward greater efficiency. Third, it would be important to understand what factors relate to quality and how quality relates to cost. This would be a necessary step toward improving the quality of human subjects compliance programs.

5. References

1. James Bell & Associates. Evaluation of NIH implementation of Section 491 of the Public Health Service Act, mandating a program of protection for research subjects. Arlington, VA: http://www.nih.gov/grants/oprr/hsp_report/hsp_final_rpt.pdf; 1998.

2. Gray BH, Cooke RA, Tannenbaum AS. Research involving human subjects. *Science*. 1978;201:1094-101.

TECHNICAL APPENDIX

This appendix describes in greater detail the cost calculations presented in the report. Three sources were used in developing these estimates. First, we relied on expert opinion. Second, we used information from the VA RDIS for fiscal year 1998, which described the number of VA studies with human subjects and the research revenues per medical center. Third, we used findings from the Bell Report,[1] under contract with OPRR.

Ratio of protocols to studies

The number of protocols reviewed dictates the optimal staffing of the IRB. No existing database captures the number of protocols that each VA medical center reviews. Hence, we had to estimate this number. Using RDIS, we obtained information on the number of human subjects studies per medical center. The average number of studies with human subjects per medical center was 123; for the high volume medical centers, the average number of studies with human subjects was 461. We know that each of these studies had to obtain IRB approval. But, if we assume that the number of protocols reviewed by each IRB is equal to the number of studies, then we would significantly underestimate the number of protocols reviewed. More often than not, an initial protocol has to be amended and re-reviewed. Sometimes this re-review is perfunctory and other times the changes are major and it is handled like a new protocol. In addition, the IRB has to review all protocols before funding is sought. If the study does not obtain research funding, then the study is often delayed or abandoned. In the end, we assumed that there were 3 protocol reviews for every ongoing study.

Assuming a ratio of 3 protocols for every ongoing study is not without merit. Expert opinion suggested that the ratio of protocols to studies was 2-3. In addition, the Bell Report found that the top 10% (n=49) of the sites reviewed on average 1,903 protocols. If we assume that the top 10% of the sites from the Bell Report are comparable to the high volume VA sites, then the ratio of protocols to studies is between 3 and 4. This assumption is further tested in the sensitivity analysis, discussed later.

Optimal allocation of committees

After estimating the number of protocols being reviewed at each medical center, we had to determine the optimal staffing needed to review these protocols. This is complicated because not all protocols take equal amounts of time to review. Luckily, we have data from the Bell Report on the time it takes to review each type of protocol Table A1.

Table A1: Percent time spent by committees reviewing protocols

	Medium volume medical center	High volume medical center
Initial review		
Full	46%	46%
exempted	13%	13%
expedited	7%	7%
Continuing	13%	13%
Amended	7%	7%
Harm reports / other issues	14%	14%
Total	*100%*	*100%*

IRBs respond to changes in workload by changing: 1) the length of each committee meeting, 2) the number of meeting per month, and 3) the number of committees. Although we recognize that medical centers might choose different paths toward this end, we assumed that committees met bi-monthly and each meeting lasted 2 hours. Experts stated that quality is maximized with meeting that are approximately two hours in length. To make our calculations tractable, we assumed that higher volume medical centers had to have more committees.

Following from Table A1, the time spent per type of protocol in a two-hour meeting is presented in Table A2.

Table A2: Time spent reviewing protocols in a two-hour committee meeting

	Medium volume medical center	High volume medical center
	(minutes)	
Initial		
full	55	55
exempted	16	16
expedited	8	8
Continuing	16	16
Amended	8	8
Harm reports / other issues	17	17
Total	*120*	*120*

The Bell Report also has information on the average time is takes a committee to review each type of protocol. Interestingly, the Bell Report found that higher volume institutions took about half the time a lower volume institution took. This could indicate differences in quality, but it could also be explained by scale efficiencies. Through repetition, high volume IRBs may be able to refine their operation, essentially following the maxim "practice makes perfect." Without data on quality, we assumed that these institutions had similar level of quality and that this difference was explained by efficiencies. Table A3 lists the review times per protocol.

Table A3: Review time per protocol

	Medium volume medical center	High volume medical center
	(minutes)	
Initial		
full	29	15
exempted	6	3
expedited	3	2
Continuing	8	4
Amended	6	3

With these data, we have the information necessary to estimate the number of reviews that are done in the average two-hour meeting. These totals are listed in Table A4.

Table A4: Number of protocols reviewed in a typical two-hour meeting

	Medium volume medical center	High volume medical center
Initial		
full	2	4
exempted	3	6
expedited	3	6
Continuing	2	4
Amended	1	3
Subtotal	*11*	*22*

We can now combine the information presented in Table A4 with data on the number of expected protocols reviewed at low and high volume VA (Table A5).

Table A5: Projected number of protocols to be reviewed by VA medical centers

	Medium volume medical center	High volume medical center
Initial	147	549
Full	87	324
exempted	422	82
expedited	38	143
Continuing	163	608
Amended	87	327
Total	*397*	*1,484*

Table A6 lists the number of committees needed to review these protocols. This was obtained by dividing the projected number of protocols by the number of each protocol that can be reviewed in a meeting (see Table A4). If we assume that there are 21 meetings a year (i.e., bimonthly with some flexibility for holidays), then we can estimate the number of committees needed.

Table A6: Estimated number of committees needed per VA medical center

	Medium volume medical center	High volume medical center
Initial		
full	2	4
exempted	0	1
expedited	1	1
Continuing	4	7
Amended	3	6
*weighted average**	*2.0*	*3.5*

* weighted by the time spent per protocol and then rounded up to the nearest half number

The weighted average number of committees in Table A6 is the crucial number. This dictates the number of committee chairs and the number of committee members. We assumed that each committee was comprised of a chair and nine committee members. Irrespective of the volume of the organization, we assumed that each organization has one FTE IRB director, one FTE administrative assistant, and one FTE computer analyst. The IRB chair, assumed to be a physician, was allocated a 0.5 FTE and committee members were assigned 0.05 FTE. The IRB director was assumed to have a Ph.D. and a base salary of $70,000 per year. Benefits were calculated at 25% of the base salary. FTE salaries, benefits and total personnel costs are listed in Table A7. If a position was only a fraction of the FTE, then the personnel cost were allocated proportionately. Recall that the number administrative staff is dictated by the number of protocols (300-350 protocols per FTE).

Table A7: Personnel costs per 100% FTE

Salary	Salary	Benefits	Total
Director, PhD	$ 75,000	$ 18,750	$ 93,750
Administrative Staff	$ 48,000	$ 12,000	$ 60,000
Administrative assistant	$ 40,000	$ 10,000	$ 50,000
Computer analyst	$ 60,000	$ 15,000	$ 75,000
Committee chair	$ 90,000	$ 22,500	$ 112,500
Committee member	$ 75,000	$ 18,750	$ 93,750

Note: No difference for high or medium volume sites.
These costs are for 100% FTE. If a position was only a fraction of the FTE, then we allocated the proportionate cost.

It should be noted that capital costs (i.e., space costs) are not included in this estimate. This would be very easy to include in the future; preliminary analysis shows that this would increase total costs by approximately 5%.

Sensitivity analysis

The largest component of the projected costs is related to personnel. Thus, assumptions that change the distribution and cost of personnel affect our estimates. We conducted a sensitivity analysis to explore which parameters affected the total costs. Most important was the ratio of protocols per study. We assumed that the ratio of protocols per study was 3:1. We then projected the costs for three other protocol to study ratios: 4:1, 2:1, 1:1 (Table A8).

Table A8: Sensitivity of projected costs to protocol to study ratio

Ratio of protocol reviews per ongoing study	Total costs	Change in total costs	Total costs per review	Change per review costs
3:1 *(baseline)*				
Medium volume VA	$ 584,134	--	$ 1,578	--
High volume VA	$ 1,009,760	--	$ 730	--
2:1				
Medium volume VA	$ 498,746	-14.6%	$ 2,021	+28.1%
High volume VA	$ 798,278	-20.9%	$ 886	+18.6%
1:1				
Medium volume VA	$ 413,357	-29.2%	$ 3,350	+112.3%
High volume VA	$ 586,795	-41.9%	$ 1,273	+74.3%
4:1				
Medium volume VA	$ 669,523	+ 14.6%	$ 1,356	-14.0%
High volume VA	$ 1,221,243	+20.9%	$ 662	-9.3%

The sensitivity analysis shows that the projected optimal costs are relatively sensitive to the ratio of protocols per study. Note that the total costs and the cost per review move in the opposite direction as the ratio of protocols per study changes. This is because there are more easy-to-review protocols relative to the number of initial full reviews. Hence as the number of protocols increases, there are relatively more easy-to-review protocols than time consuming ones. The total costs increase at a slower rate than the number of protocols, thus the cost per protocol is declining.

With regard to the cost per review, if we assume that there is only one protocol per study, then the cost per protocol is $3,350 and $1,273 for the high volume and medium volume VA, respectively. In some sense, this provides us with an upper bound. We know that this estimate exaggerates the cost per protocol, but the exact amount is not known. Further research is needed to provide more exact cost estimates.