Regulatory compliance an increasing burden on sites

Increased staff time, materials, storage eroding site operating profit

By Ronald Rosenberg
Staff Writer

As the biopharmaceutical industry strives to reduce its R&D costs and shorten timelines, it must face the fact that today’s successful drug development plans often require more clinical studies than they did a dozen years ago.

Often that translates to more complex clinical trials for investigative sites, requiring pre-screening of larger patient pools, more personalized data and time-consuming and complex regulatory compliance. Site non-compliance with Good Clinical Practices (GCP) has been rising; many sites have said the regulatory burden continues to increase as study timelines continue to slip.

But unlike the pharmaceutical industry, many sites continue to operate as a cottage industry, lacking the cohesiveness and financial resources to improve efficiency and flexibility.

While there is wide agreement that the regulatory compliance burden for sites is high, few initiatives have been launched in the industry and little to no data exists to quantify this regulatory compliance burden on sites.

But a new CenterWatch survey, sponsored by Complion, sheds some light for the first time on how, and how well, sites manage regulatory compliance.

Complion, a Cleveland-based software development firm for sites and site networks that creates software for electronically recording essential clinical trial regulatory documentation, recently surveyed 164 site personnel. The results have been released in 2014 Regulatory Compliance Practices.

Respondents included independent research centers (10% of the total sample size), sites affiliated with Academic Medical Centers (35%), private practice sites (23%), sites affiliated with community hospitals (27%) and other sites (5%). More than half of the survey respondents were Study Coordinators/study nurses, while 20% were Principal Investigators. Other respondents included regulatory specialists, administrators and managers.

Time required

The survey found Study Coordinators and nurses, often the primary managers of regulatory compliance for sites, juggle a significant amount of work when factoring in all of their responsibilities. Interestingly, the survey found staff time for most regulatory tasks did not differ significantly across the different site types.

“We were specifically interested in a range of things, from staffing requirements to managing site regulatory compliance, the formats used in storage and exchange of regulatory documents, the costs related to maintaining compliance, plus the inefficiencies that are a burden on sites,” said Rick Arlow, CEO of Complion. “What stood out is that over a two-month clinical trial period, one-third of the time is spent on regulatory

<table>
<thead>
<tr>
<th>Factors contributing to increased regulatory cost/burden</th>
<th>Percent mentioning</th>
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<tbody>
<tr>
<td>Increased regulatory requirements</td>
<td>73%</td>
</tr>
<tr>
<td>Increased protocol complexity</td>
<td>66%</td>
</tr>
<tr>
<td>Increased site responsibilities</td>
<td>61%</td>
</tr>
<tr>
<td>Increased reporting requirements (adverse event reporting/deviations/etc.)</td>
<td>53%</td>
</tr>
<tr>
<td>Increased protocol amendments</td>
<td>53%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
</tr>
</tbody>
</table>

Source: CenterWatch-Complion study, 2015; N= 164 investigative sites
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CenterWatch Publications and Services

Clinical Trials Data Library
A valuable online resource providing access to comprehensive charts and tables on the life sciences and clinical research industry.

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Research Practitioner
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JobWatch
A web-based service featuring clinical research jobs, career resources and a searchable resume database.

Drugs in Clinical Trials Database
A searchable database of 4,000+ detailed profiles of new drugs in development. CenterWatch also prepares custom drug intelligence reports covering a variety of medical conditions.

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- Protecting Study Volunteers in Research, 4th Ed.
- The CRA’s Guide to Monitoring Clinical Research, 3rd Ed.
- The CRC’s Guide to Coordinating Clinical Research, 2nd Ed.
- The PI’s Guide to Conducting Clinical Research
- SOPs for Clinical Research
- SOPs for Sponsors
- SOPs for Medical Device Sponsors—New

Primary manager of regulatory compliance tasks

<table>
<thead>
<tr>
<th></th>
<th>Principal Investigator</th>
<th>Sub-investigator</th>
<th>Study Investigator/Study Nurse</th>
<th>Regulatory Specialist</th>
<th>Administrator</th>
<th>All other</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>3%</td>
<td>2%</td>
<td>5%</td>
<td>4%</td>
<td>4%</td>
<td>22%</td>
</tr>
<tr>
<td>Independent</td>
<td>16%</td>
<td>46%</td>
<td>57%</td>
<td>4%</td>
<td>51%</td>
<td>70%</td>
</tr>
<tr>
<td>AMCs</td>
<td>16%</td>
<td>28%</td>
<td>29%</td>
<td>4%</td>
<td>25%</td>
<td>4%</td>
</tr>
<tr>
<td>Community Hospitals</td>
<td>4%</td>
<td>7%</td>
<td>5%</td>
<td>4%</td>
<td>4%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Source: CenterWatch-Complion study, 2015; N= 164 investigative sites

tasks, and the rest was on routine information maintenance. So we see big opportunities for improvement with a streamlined process in which some clerical tasks don’t need to exist.”

Still, that is a disproportionately large amount of time spent on regulatory compliance, which leaves less time for activities such as patient recruitment. For a typical clinical study, site staffs spend a median 34 hours on clerical activities, 36 hours on regulatory work and 44 hours on sponsor/CRO-related activities.

Of that median 114-hour total of regulatory, clerical and sponsor/CRO tasks, the most time consuming were:
- 11 hours for training associated with learning sponsor/CRO’s investigator or regulatory web portals
- 10 hours for monitoring or audit visit follow up
- 10 hours of protocol-specific training of staff
- 9 hours for reviewing regulatory documentation with monitor or auditor
- 9 hours for reviewing correspondence
- 8 hours of GCP training of staff.

Many of those tasks also raise the total regulatory cost/burden associated with a single clinical trial, which has risen over the past two years, due primarily to increases in regulatory requirements, protocol complexity, site responsibilities, protocol amendments and reporting requirements, such as adverse event reporting/deviations.

Staff and training

For 46% of respondents in private practice sites, the Study Coordinator/study nurse is the primary manager of regulatory compliance tasks. In academic and community hospital sites, 28% of respondents have a regulatory specialist. In general, two staff members manage all of the regulatory compliance in private practice and independent research centers, while both academic and community hospitals have three staffers.

According to 60% of respondents, one person can effectively manage regulatory compliance tasks in addition to other study responsibilities for as many as four studies. About 75% of respondents said one person with primary responsibility for compliance could effectively manage the tasks for five or more studies. The survey also noted AMCs are more likely to use internal processes to manage regulatory compliance, while private practice sites would follow sponsor procedures.

Asked how far behind schedule sites typically are on the maintenance of the regulatory tasks, prior to an audit or monitoring visit, less than half of all sites—46%—said they were on schedule, while 28% were less than a week behind and 14% were two weeks behind.
Some site executives question the need for repetitive GCP training of site staff as unnecessary, citing TransCelerate’s call for GCP training only once every three years. “Those GCP modules are window dressing, because the most important thing—the science—is lost in the noise,” said Michael Koren, M.D., a cardiologist and CEO of the Jacksonville Center for Clinical Research. “This change in reducing the amount of GCP training is happening painfully slowly. A few weeks ago, I got eight requests for GCP training and I’m board certified in GCP!”

He is not alone, as others agree routine GCP training for experienced site staff is unfair and unnecessary. “Frankly, it’s a staggering waste of time doing GCP training for every study and takes away core hours that could be spent on revenue-generating activities,” said Terri Hinkley, interim executive director of ACRP.

Staff and material costs

A key part of the survey dealt with the total cost of regulatory tasks—staff time plus material costs—for a single study. The median estimate among 55 respondents was $6,000. However, the survey found for an average 24-month study, the actual costs—from startup to database lock—took an estimated at 255.5 hours of staff time (at $50 per hour) for a cost of $12,755. Add to that an estimated $1,226 in materials—paper, folders, binders, storage boxes, document storage and regulatory software—the total cost is $13,901, more than double the median estimate.

“Many sites need to better estimate their true costs,” said Hinkley. “We have to provide the sites with the tools to do forecasting accurately so it is built into the study for them to be sufficiently compensated.”

But others cited sponsors’ attempts to avoid paying unexpected additional site expenses.

“From the site perspective, we are getting stuck with additional costs, but in talking to some of the sponsors’ contracts people they have a different explanation,” said Bill Smith, CEO of New Orleans Clinical Research (NOCCR) and Volunteer Research Group, which has a $13,000 to $15,000 start-up cost. “They have a system and there is no place to put these additional costs, as the template they use with sites has not anticipated them.”

Space and storage

Another widely cited concern is document storage. Sites have to physically store voluminous records and absorb most of those archiving costs, often for 11 or more years. The predominant storage format across all types of clinical study documentation is a combination of paper and electronic. The survey found 44% of respondents cited exchanging IRB submission documents with their IRB using electronic formats, compared to 48% that used a hybrid of paper and electronic formats. The most commonly used method for the exchange of regulatory documents is email, followed by a sponsor/CRO web portal and fax.

Fifty-one percent of respondents said their sites dedicate up to 16% of their physical office space to storage of paper regulatory documents, which also can include printouts of emails. One third said they set aside 25% or more for office space storage.

More than half—54%—also said four or more binders are used to store regulatory documents for a single study, and most said these documents exceed 250 pages. Nearly 60% of respondents said their storage binders typically are more than 500 pages.

Augmenting in-house storage are outside
companies that archive clinical study documents for the majority of sites.

“It’s a great idea to have less paper and more electronic records to store documents, but my skepticism is based on how well we get the FDA to address these issues,” said Mark Lacy, founder and CEO of Benchmark Research.

Reimbursement

One of the most nagging problems for sites is the inadequate reimbursements they receive from sponsors. According to 79% of survey respondents, the amount sponsors provide for start-up costs does not sufficiently cover all regulatory compliance expenses.

Additional expenses typically not covered by sponsors include ongoing regulatory compliance, staff training on regulatory compliance and training associated with learning sponsor/CRO web portals.

One exception cited in the survey report was for AMCs, which said they received a $290 reimbursement from sponsors on $2,000 in estimated regulatory maintenance costs.

Sites are reimbursed a median $3,000, about 80% of the median estimated regulatory start-up cost of $3,750. They also receive a median $500 for document storage, about 50% of the median archiving cost of $1,000.

“We now supply all the paper and most of the binders required for storage of documents,” said one survey respondent. “These binders can cost up to $20 each. They used to be supplied to us. I have increased our required overhead charge in budgets to help cover additional costs, but most companies max out at 25% overhead and I am not sure that really covers all of our costs.”

Key areas for improvement

Three-quarters of respondents cited additional sponsor reimbursement and support for regulatory compliance costs as key areas for improvement. They also urged for a reduction in documentation storage space and storage options, lower material costs, better training and a more efficient process for clerical regulatory tasks. Among the most time-consuming clerical activities: an average of 7.4 hours spent filing credentials and CVs—nearly all on paper—which could be reduced sharply with online documentation.

But it is clear from the survey results that sites cannot handle any increased burden in the regulatory compliance process. And they must better handle the existing burden, by setting more realistic cost estimates, informing sponsors upfront that their start-up budgets to not cover all necessary and ongoing regulatory and storage costs.

“Sites may be underestimating the extent of the staff time involved in regulatory compliance,” the survey report stated. “And as a consequence, most likely are underestimating the overall regulatory costs in general when calculating their study budgets. Staff time related to regulatory compliance tasks is a substantial cost factor—significantly more so than the material costs. When staff time is accounted for by individual regulatory-related task and subsequently aggregated, the total cost is considerable.”

Converting to an all-electronic format and eliminating paper documents is the path forward. Similarly, the report concluded, the high number of binders, regulatory pages and correspondence linked with a single trial suggests a labor-intensive, potentially inefficient regulatory compliance process.

“Streamlining the regulatory process across studies through the establishment of universal guidelines or standardized processes accepted by all key stakeholders (e.g., sponsors, CROs, sites, IRBs),” the report found, “is viewed by many sites as an avenue to an enhanced regulatory compliance process overall.”

Some sites say smaller sites are losing ground in meeting the expanding workload requirements, as larger sites have dedicated patient recruitment, regulatory staff and clinical coordinators to meet increasing demands. Others point to the need for greater standardization on electronic data capture and electronic medical record systems to reduce the need to learn a variety of different sponsors’ systems.

“More electronic technology to save time and money is needed, because trials are not getting easier and, in some ways, they are more cumbersome,” said Laurie Jassenoff, vice president of Palm Beach Research. “We need to make more than adjustments to lower the regulatory burden. Overall communications with sponsors and CROs also must improve, along with improved efficiencies. Those changes can be made.”

### Actual v. estimated costs associated with regulatory tasks

<table>
<thead>
<tr>
<th>Costs associated with regulatory tasks</th>
<th>Estimated cost per single clinical study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total estimated costs</td>
<td>$6,550</td>
</tr>
<tr>
<td>Amount reimbursed by sponsor</td>
<td>$3,500</td>
</tr>
<tr>
<td>Actual staff time costs (based on itemized analysis)</td>
<td>$12,775</td>
</tr>
<tr>
<td>Total material costs (based on itemized analysis)</td>
<td>$1,126</td>
</tr>
<tr>
<td><strong>TOTAL ACTUAL COST</strong></td>
<td><strong>$13,901</strong></td>
</tr>
</tbody>
</table>

*Average months from study startup to database lock = 24 months, estimated 255.5 hours of staff time for regulatory-related tasks per single clinical study, Fair Market Value for CRC or Regulatory Specialist estimated at $50/hour

Source: CenterWatch-Complion study, 2015; N = 164 investigative sites