

## Preventing Overlapping Enrollment in Clinical Studies

By Darran Boyar and Norman M. Goldfarb

The lack of a national (or international) registry of clinical study subjects means that nobody knows how many people enroll in overlapping studies. If a person enrolls in two or more overlapping studies (including waiting periods), serious ramifications may include injury to the subject from concurrent medications, invalid study data (including mysterious adverse events), and wasted time and money replacing subjects that are found to be ineligible. Further, the public relies on valid clinical trials to make the right drugs and medical devices available. The overlapping enrollment problem is most common in Phase I clinical research because of the nature of the population and higher levels of compensation, but it is likely a problem in other phases of research as well.<sup>1,2,3,4</sup>

A single web-based national registry for all clinical study subjects would make tremendous strides toward eliminating this problematic behavior. Current subject identifiers, such as initials and date of birth, can be used to flag potential problems, but they lack discrimination. Adding the subject's gender and the last four digits of his or her Social Security number almost certainly identifies unique individuals. However, to be sure the person is being honest about his or her identity, a biometric identifier is required. Fortunately, high-quality fingerprint scanners that cost about \$100 in volume are available as accessories to personal computers. This technology can generate a numeric code from each fingerprint, which works well for cross-matching and avoids the privacy issues that would result from storing fingerprints in the database. False acceptance and rejection rates with such fingerprint systems are extremely low: 0.0003% and 0.1%, respectively.

In the U.S., a study subject registry must comply with federal privacy rules: the Health Insurance Portability and Accountability Act (HIPAA) and the Code of Federal Regulations (21 CFR Part 11).<sup>5,6</sup> Many states also have their own privacy regulations, but a registry that complies with the federal regulations should meet most or all of these requirements as well. Security measures should include:

- Secure login to authenticate identity of users of the system
- A secure Internet connection
- Use of encrypted passwords with adequate strength and auto-expiry
- Audit trail for traceability

The registry should also support seamless integration with an institution's existing software infrastructure in a way that does not inappropriately access proprietary or confidential information. Potential subjects must sign a HIPAA release form authorizing collection and use of their data for the registry's purpose.

A national study subject registry would add a small amount to the current cost per subject. A public/private

partnership could easily cover the cost of creating and operating the system with grants and usage fees.

## Results and Discussion

In 2009, five clinical research sites in South Florida joined together to address their concern about overlapping enrollment. They commissioned Independent Data Integrator (IDI), a company specializing in clinical database management, to create a subject registry. IDI

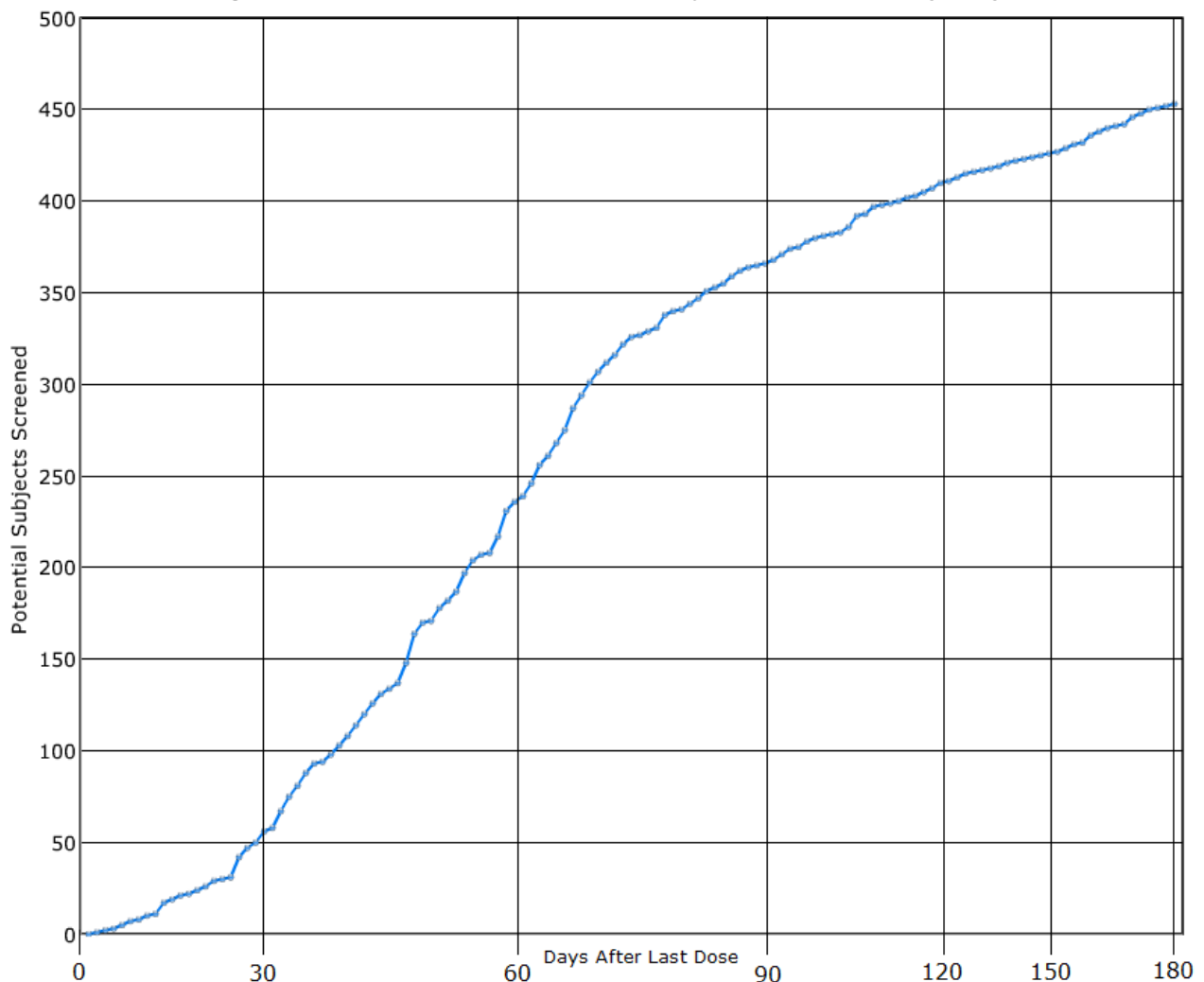
developed a system called Clinical Research Subject Verification Program, or clinicalRSVP. All five sites continue to subscribe to the service. Meanwhile, IDI has collected and analyzed data to assess the frequency of possible overlapping enrollment.

Study coordinators at the five sites entered the demographic and biometric identifiers mentioned above. For enrolled subjects, Most Recent Dose Taken Date and Scheduled Final Dose Date (if any) were also entered within 18 hours after the subject's first and last doses. If a subject left a study prematurely, that data was also entered. It took less than five minutes per potential subject to collect the registry data, enter it into clinicalRSVP, and obtain the result.

During the 18-week data collection period starting in November 2009, the five sites conducted 27 Phase I studies. They registered 2,081 potential subjects. As shown in Figure 1, 453 individuals (21.8%) attempted to enroll in a second study. Of these, 50 (0.25%) individuals attempted to enroll within 30 days of receiving a dose in a previous study, and an additional 186 (0.9%) attempted to enroll within 60 days.

Two large research sites in the local area did not participate. If they had, these percentages would have been higher. Significantly, before a potential subject was screened for a second study, he or she signed a form *for the second time* informing him or her of the clinicalRSVP

**Figure 1. Cumulative Potential Subjects Screened by Day**



registry. Presumably, knowledge of the registry discouraged some potential subjects from attempting to enroll in a second, overlapping study.

Phase I trials generally require subjects to have not participated in another study for 30 days prior to enrollment, but the eligibility criteria for these studies is unknown to the authors. The 50 subjects screened within 30 days after dosing were probably rejected based on clinicalRSVP screening, but it is unknown how many others were also rejected for this reason. An additional 10 to 20 subjects were rejected by sites for having enrolled in another study after initial screening and before first dosing. It is unknown how these results relate to later-phase trials or other geographical areas. Although some useful data is not available to the authors, it is clear that a significant number of study subjects nationwide are enrolling in overlapping studies. Further research is required to determine more accurately the percentage of potential subjects who attempt to enroll in overlapping studies.

## Conclusion

The general public, clinical research subjects, sites, and sponsors would all benefit from a national registry of study subjects. As this study has shown, even local registries can be effective in deterring overlapping enrollment, resulting in improved subject safety and research integrity.

A national, comprehensive, web-based registry of study subjects would offer the following advantages:

- Capture of study subjects across all participating research sites
- Standardized timing and processes for screening potential subjects
- Standardized data elements and process for data entry, reporting, management and validation
- Established rules for regulatory and institutional review board (IRB) compliance
- Lower cost
- Knowledge about clinical study participation rates

Even without a national system, local systems can be effective.

## References

1. Lemonick M., Goldstein A. At Your Own Risk, *Time*, April 22, 2002, pp. 56.
2. Drug Test Human Guinea Pigs, *Drug-Test Dummies*, *Men's Health*, <http://www.menshealth.com/men/health/other-diseases-ailments/drug-test-human-guinea-pigs/article/3f4aeb53bd0a8110vgnvcm20000012281eac>, accessed February 24, 2010.
3. Evans D., Smith M., Willen L. Big Pharma's Shameful Secret, *Bloomberg Markets*, December 2005.
4. Tishler C., Bartholomae S. Repeat Participation Among Normal Healthy Research Volunteers: Professional Guinea Pigs in Clinical Trials?, *Perspectives in Biology and Medicine*, Autumn 2003; 46(4), pp. 508-20, [http://muse.jhu.edu/login?uri=/journals/perspectives\\_in\\_biology\\_and\\_medicine/v046/46.4tishler.html](http://muse.jhu.edu/login?uri=/journals/perspectives_in_biology_and_medicine/v046/46.4tishler.html), accessed February 24, 2010.
5. 21 Code of Federal Regulations (CFR) Part 11: Electronic Records; Electronic Signatures, <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=11>, accessed February 24, 2010.

6. Understanding HIPAA Privacy, U.S. Department of Health & Human Services, <http://www.hhs.gov/ocr/privacy/hipaa/understanding/index.html>, accessed February 24, 2010.

### **Authors**

Darran Boyer is President and CEO of Independent Data Integrator LLC. Contact him at 1.888.308.778 or [darran.boyer@clinicalrsvp.com](mailto:darran.boyer@clinicalrsvp.com)

Norman M. Goldfarb is Managing Director of First Clinical Research LLC, a provider of clinical research best practices information, consulting and training services. Contact him at 1.650.465.0119 or [ngoldfarb@firstclinical.com](mailto:ngoldfarb@firstclinical.com).