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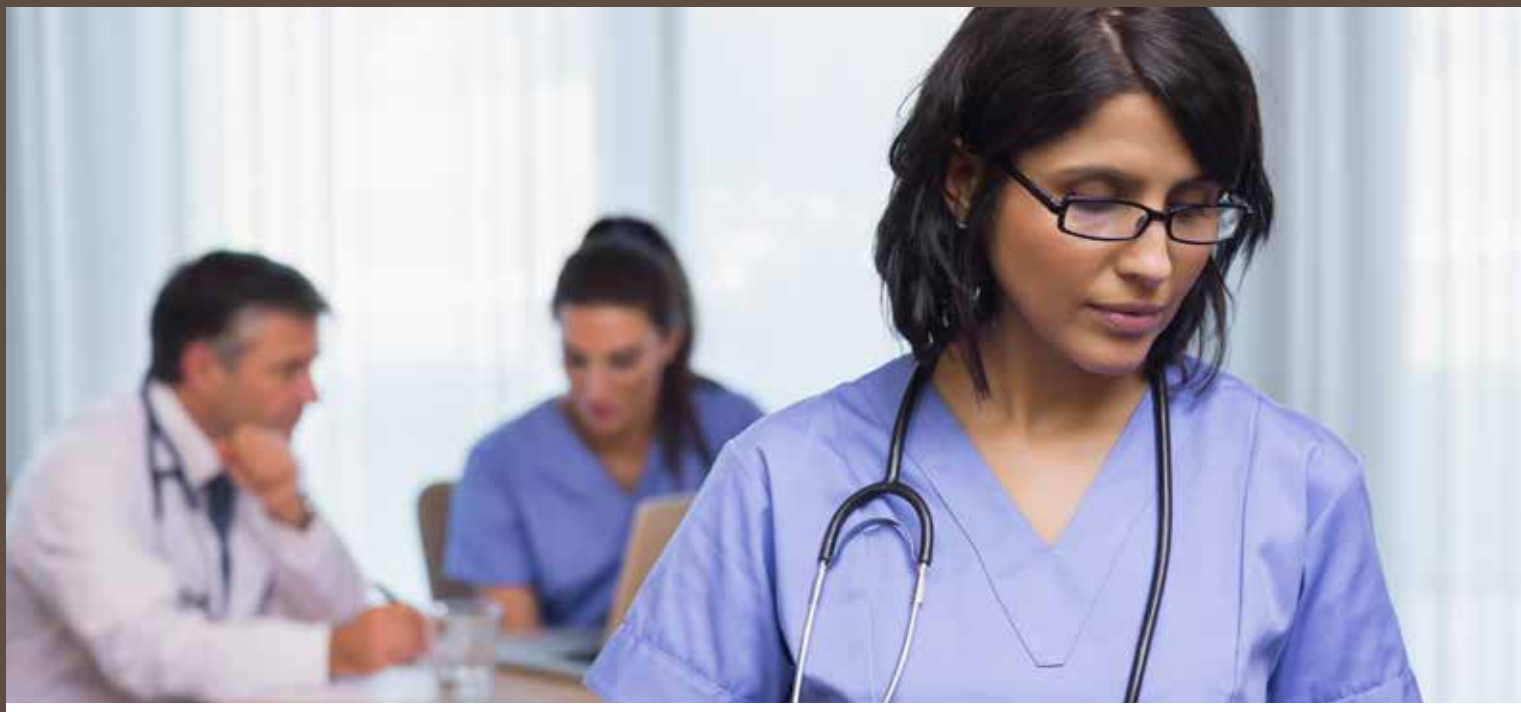

LESSONS FROM INDIA

In just a year, India has changed from a preferred location for large clinical trials to a country with shrinking popularity among Pharmaceutical and Medical Device sponsors of clinical research. An "uncertain regulatory environment" is most often cited as the driver of India's bruised research profile. That uncertainty continues as India struggles to develop a new regulatory framework for clinical research.

India's experience with clinical trials regulation and monitoring may provide insight into some pressures faced by other countries with regulatory systems racing to keep up with the countries' skyrocketing Life Science industries. In India, the primary driver of regulatory reform is the country's Supreme Court, which expressed strong concern about the safety of India's participants in clinical studies when it instructed the government to reform the country's clinical trials regulatory framework.

The regulatory uncertainty associated with the Court's instruction led many sponsors to stop or delay trials in India while they waited to see the government's plans for reform. The Court, annoyed by the slow response of the government, made rulings that effectively set new regulatory standards. One of the most important developments to come from the Court is its mandate that informed consent be videotaped and that victims of clinical trials be

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LESSONS FROM INDIA *(Continued)*

adequately compensated for their injuries. The Court has given broad definitions of "victim" and "injuries," causing concern to some sponsors of long-term financial liability. Perhaps most important, the Court has tackled an issue common to all locations with large, treatment-naïve populations – exactly the potential patient pool sought for clinical trials – by requiring that informed consent be videotaped. Other countries, including the US, are likely to at least consider similar measures as a way of addressing growing concerns about uninformed or inadequately informed study participants in clinical trials.

The proposals in India may resonate with regulators in other countries and potentially increase the complexity of clinical trials even beyond India's borders. Among the proposals most closely watched is CDSCO's draft guidance on financial compensation for clinical trial participants (draft "Guidance for Financial Compensation to be Paid in Case of Clinical Trial Related Injury or Death"). This Draft proposes:

- Sponsor companies and clinical research organizations that failed to comply with the required compensation to volunteers in cases of trial-related deaths or injuries could face suspension of trials or even permanent bans;
- The procedure for complying with the notification requirements is complex, involving several detailed steps before the Independent Ethics Committee established by the Drug Controller General of India makes a case-by-case determination of the amount of compensation for the reported trial-related injury or death.

Several industry organizations including the Indian Society for Clinical Research (ISCR) have expressed concern about the ambiguities of the proposed compensation guidelines. One concern is the absence of distinction between a study-related injury and a non-related injury that a clinical trial subject might experience and the requirement that the subject receive free medical management for as long as necessary. A second concern comes from patient entitlement to compensation for injury or death due to issues ranging from violations of the approved protocol, to misconduct of the sponsor or investigator, to failure of the investigational product to provide the intended therapeutic effect, or the use of placebo in placebo-controlled trials.

Several of the recommendations appear to conflict with the purpose of a clinical trial. For example, Indian GCP guidelines define a clinical trial as a "... study of pharmaceutical products on human subjects ... in order to discover or verify the clinical, pharmacological ... and/or adverse effects, with the object of determining their safety and/or efficacy." In placebo-controlled trials, a placebo is not meant to have any therapeutic effect. Indian placebo-controlled trials are closely evaluated by the New Drug Advisory Committee (NDAC) prior to approval to satisfy that the trial will not be detrimental to the safety of the subjects. An additional safeguard is the Ethics Committee, which traditionally has responsibility to determine if the protocol supports placebo use and whether there are sufficient mechanisms for patient monitoring.

There is universal agreement that sponsors have obligations to ensure safe and ethical conduct of its clinical trials. Every country is justified in overseeing the conduct of its research community to ensure compliance with GCP requirements. India's proposed guidelines, however, may have the opposite effect the government intends by discouraging future Pharmaceutical and Medical Device clinical studies in the country. The clinical research community – as well as regulatory bodies in other countries – will be paying close attention to the proposed regulations and the global clinical research community.

THE WCG ACADEMY LIFTS OFF

The PRIM&R (Public Responsibility in Medicine and Research) Advancing Ethical Research (AER) Conference was the site for the launch of the WCG Academy, which is the result of a partnership between UL EduNeering and the WIRB-Copernicus Group (WCG). WCG is the world's largest provider of regulatory and ethical review services for human research, with eight AAHRPP-accredited panels and more than 100 experienced board members.

The WCG Academy provides IRB and clinical research professionals with required regulatory and ethics education. Expert and level-appropriate content has been developed by WCG to address training needs for CFR 21 Part 54, CFR 42 Part 93, and CFR 45 Part 46. In addition, the WCG Academy contains a custom set of GCP courses from UL EduNeering's extensive Life Science library, including courses used by FDA in its online university (ORA-U) to train federal, state, local and foreign inspectors.

ComplianceWire®, an easily accessible, online knowledge solution from UL EduNeering, uses highly tailored, role-based curricula to address the knowledge and certification needs of IRB reviewers, members, staff, and investigators and their teams. ComplianceWire technology delivers, manages and tracks learners across institutions, sponsors and clinical trials. Both learners and staff responsible for monitoring certification records can now access a single source for aggregated reporting of relevant training.

According to Lynne Budnovitch, General Manager of UL EduNeering, "WCG Academy leverages our 30 years' experience in Life Science learning to unify the delivery, management and tracking of clinical research qualification certifications in our validated and cloud-based ComplianceWire platform."

"Our goal is to improve the clinical trial start-up process by integrating ethics and GCP education into a comprehensive set of protocol and IRB-related services", says Nick Slack, Senior VP, Strategic Partnerships. "WCG Academy will help improve quality and compliance in study conduct through provider-appropriate training to all clinical professionals engaged in human research."

The AER conference was a fitting backdrop for the launch of the WCG Academy. The Conference featured presentations from respected subject matter experts addressing issues that ranged from global research ethics to evolving techniques in adult learning.

TOWARD A TRANSPARENT FUTURE

It's unlikely that the European Medicines Agency (EMA) expected the kind of response it received when it opened its draft transparency policy for clinical trials to public comment last June. The response – more than 1,000 comments over three months – indicates just how important the issue of transparency is to stakeholders ranging from patients to advocacy groups, the clinical research community and government regulators.

EMA's June 2013 release of its draft for publication and access to clinical trial data came with the explanation, "There is a growing demand from external stakeholders for full transparency, not only about the Agency's deliberations and actions, but also about the data and results from clinical trials on which regulatory decisions are based."

The response generated by EMA's open comment period reinforces recent events related to clinical trial transparency. In May 2013, US Representative Ed Market (D, MA) introduced HR 2031 (Trial and Experimental Studies Transparency Act of 2012, or the TEST Act). The Act would amend the Public Health Service Act to expand clinical trials that must be reported to the clinical trial registry data bank. Among the trials that would be included are any interventional study of a drug, device, or biological product conducted outside of the United States the results of which are submitted to the Secretary of Health and Human Services (HHS) as support for approval of an application; and post market surveillance of a class II or class III device that involves data collection from human subjects.

Increasing the transparency of clinical trials isn't limited to regulatory agencies, however. In December 2013, Pfizer announced a new data sharing policy that makes information from its sponsored clinical trials available. According to the company, it will launch a portal in January 2014 allowing qualified researchers to access data from completed trials of approved drugs.

The private-sector and public-sector push toward greater transparency of clinical trials is unlikely to abate. Even though the EMA's final regulation and the TEST Act in the US remain incomplete, the trend is unmistakable and can be expected to affect all clinical trials, regardless of where they are performed.

About UL EduNeering

UL EduNeering is a business line within UL Life & Health's Business Unit. UL is a global independent safety science company offering expertise across five key strategic businesses: Life & Health, Product Safety, Environment, Verification Services and Enterprise Services.

UL EduNeering develops technology-driven solutions to help organizations mitigate risks, improve business performance and establish qualification and training programs through a proprietary, cloud-based platform, ComplianceWire®.

For more than 30 years, UL has served corporate and government customers in the Life Science, Health Care, Energy and Industrial sectors. Our global quality and compliance management approach integrates ComplianceWire, training content and advisory services, enabling clients to align learning strategies with their quality and compliance objectives.

Since 1999, under a unique partnership with the FDA's Office of Regulatory Affairs (ORA), UL has provided the online training, documentation tracking and 21 CFR Part 11-validated platform for ORA-U, the FDA's virtual university. Additionally, UL maintains exclusive partnerships with leading regulatory and industry trade organizations, including AdvaMed, the Drug Information Association, the Personal Care Products Council and the Duke Clinical Research Institute.