EU lawmakers last month approved a compromise proposal for a new clinical trials regulation, paving the way for a March 10 plenary debate and adoption of a single regulatory framework for all 28 member states before upcoming May elections.

The measure, originally introduced by the European Commission in 2012, would replace the current clinical trials directive with a regulation that does not have to be transposed by each of the 28 EU member states. Among its aims are to standardize clinical trial rules across member states and increase trial transparency — a goal that syncs with the European Medicines Agency’s push to boost access to trial data.

Key changes from the version voted out of the Committee on the Environment, Public Health and Food Safety last June (IPRM, June 2013) include:

- An allowance for sponsors seeking marketing authorization to register trials through a single, publicly accessible EU database managed by the EMA;
- The establishment of a single authorization procedure for all clinical trials to speed reviews of applications filed in more than one member state; and
- Greater uniformity of review times for applications across member states.

The proposed draft also would expand informed consent procedures and establish mechanisms allowing the European Commission to intervene in member states or third countries to ensure the clinical trial rules are properly supervised and enforced.

Erik Vollebregt of Axon Lawyers in the Netherlands says the Dec. 20 compromise “was reached to speed up the [legislative] process and iron out some of the political kinks to be able to finish the regulation before the May 2014 elections. They did this because all involved would like to claim some success in the healthcare field with, for example, the medical devices regulation [being] dead in the water after the 10 December EPSCO council.”

The European Federation of Pharmaceutical Industries and Associations applauded the compromise — in particular, new timelines for trial authorizations. Once approved, national authorities would have 60 days to approve a trial; the deadline
could be extended another 50 days for certain complex drug products.

But EuropaBio questioned whether the proposed timelines are aggressive enough to boost medical research in Europe. “These extended timelines lack ambition and signal that there is little commitment to restoring a competitive environment for conducting clinical research in Europe,” the trade group said. “Including the timelines for questions and assessment of responses, the total assessment timelines would actually be nearer to or in many cases exceeding 100 days.”

**Transparency Provisions**

On transparency, the Dec. 20 draft regulation tracks closely with EMA plans to increase public access to clinical trial data. Implementation of the EMA initiative, originally set to take effect Jan. 1, has been delayed until after a meeting slated for March.

Under last month’s compromise language, sponsors would have to publish summary results of clinical trials to the EU database in layperson terms within a year of completing a trial. Sponsors would also have to submit clinical study reports within 30 days of receiving marketing authorization. Sponsors that withdraw applications would still need to submit those reports to the EU database.

A key point of contention with industry has been the potential release of private patient data and commercially confidential information. The draft reiterates the EMA’s position that CCIs cannot be considered confidential in light of public interest (*IPRM*, July 2013).

However, the draft does make certain exceptions, such as when it is necessary to protect patient privacy or protect communication between member states in relation to the preparation of assessment reports. It is unclear how the EMA plan would address the assessment reports issue.

EFPIA welcomed lawmakers’ approach on the issue, saying it reflects EFPIA and PhRMA principles regarding “responsible” data sharing with researchers, patients and the public.

Ben Goldacre, a transparency advocate and outspoken industry critic, called the vote “exciting news,” but noted that the vast majority of drugs currently on the market won’t be covered, possibly for a generation, even if the regulation is adopted. Neither the regulation nor the EMA’s transparency plan would apply retroactively to most drugs that have already been authorized.


— Ferdous Al-Faruque

### Brazil Establishes Comprehensive Track-and-Trace System for Drugs

Drugmakers that market products in Brazil have two years to present Anvisa with a full report of traceability of at least three batches, according to a resolution published in the Dec. 11 Official Journal. The resolution establishes a framework for a National System of Drug Control that will enable the track and trace of medicines from production to the final consumer.

By Dec. 11, 2016, labels of all drugs marketed and distributed in Brazil must display a two-dimensional barcode comprising a 13-digit codified series of numeric or alphanumeric characters. The unique identifier must appear on all levels of packaging and be accompanied by the drug’s batch and serial numbers and expiry date, the resolution says.

Drugmakers are required to maintain records of a product’s movement through the supply chain for at least one year following the product’s expiry, the resolution says. A real-time database must be established on all movements of a drug, including the establishment receiving it, trucking companies, date and nature of each move in the supply chain and the code identifier of the transport packaging.

Distributors must also maintain, in real time, information on the flow of drugs. The information should include
the unique identifier, manufacturer and receiver of the drug and transport companies involved in moving the drug.

Anvisa has scheduled a Jan. 23 public hearing to discuss the creation and implementation of a Traceability Systems Technical Committee, which will monitor implementation of the national drug control system.

The resolution is available, in Portuguese, at www.fdanews.com/ext/resources/files/01/01-14-Anvisa.pdf.
— Meg Bryant

**Pharma 2013: Transparency, Clinical Trials, Bribery Dominate the News**

**Transparency and bribery — ying and yang — all but dominated global pharmaceutical headlines in 2013.** “Sunshine” was cast on regulatory authorities and drugmakers in the U.S. and European Union. A number of industry associations and some individual companies also took steps to operate more transparently. The moves came as a major bribery scandal made waves in China, bringing pressure for more punishing antibribery rules. Meanwhile, the EU and India pushed forward with new clinical trial controls, and U.S. track-and-trace efforts advanced. With 2014’s script still a work in progress, take a look back at 2013 and use its lessons to plan your business strategy for the coming year.

**EU Pushes Transparency.** Hot off the heels of implementing new pharmacovigilance legislation in 2012, the European Medicines Agency took steps last year to further secure the drug supply chain, adding sunshine to its regulatory practices by publishing the minutes and agendas for its Committee for Medicinal Products for Human Use and Committee for Advanced Therapies. The agency also pressed for greater transparency of clinical trial data.

But the move for greater transparency in clinical research hit some road bumps during the year. The General Court of the European Union issued a temporary injunction barring the EMA from releasing data following lawsuits challenging an agency decision to make public clinical trial data on every drug product.

In December, the EMA was postponing any further consideration of the controversial plan until after a March management meeting.

Separately, the European Parliament’s Committee on Civil Liberties, Justice and Home Affairs considered a proposed regulation to enhance user-data protection. If adopted, it would require drugmakers needing to transfer data out of Europe for approval purposes in other regulatory jurisdictions to first obtain authorization from existing data protection authorities and trial participants. The proposal also includes limits on profiling a person’s health, only allowing profiling by consent, when provided by law or when needed to pursue a contract.

**India Ramps Up Controls of Clinical Trials.** Reeling from charges that new drugs were approved without human testing and a three-month court-imposed hold on clinical trials, India’s Ministry of Health and Family Welfare issued a final rule clarifying the responsibilities of local licensing authorities and the Central Drugs Standard Control Organization in authorizing clinical trials in the country. The rule followed new rules on trial compensation, suggesting the government is taking seriously demands that it clean up its act.

The ensuing months brought cries from peers and industry to scale back some of the more extreme measures, such as compensatory entitlement for deaths that occur in trial. Concerns with the compensation rules led the U.S. National Institutes of Health to withdraw trial research in India.

In August, the health ministry introduced legislation overhauling the regulatory frameworks for clinical trials, drugs and medical devices. The bill dovetailed with news that the ministry plans to scale back certain elements of its trial compensation rules. The revised plan would retain compensation for subjects injured in trials, but eliminate mandated compensation for study subjects who receive no therapeutic benefit from a trial.

While the compensation rules seem here to stay, the regulatory overhaul bill was short-lived. In December, a committee in Parliament rejected the proposal, saying the plan to create a Central Drugs Authority was “unacceptable.” The bill called for the CDA to be overseen by a council of permanent secretaries from related ministries.

**China, Brazil Crack Down on Bribery.** Scandals erupted following accusations that executives with GlaxoSmithKline bribed Chinese government officials through kickbacks. In the months following those charges, Chinese officials probed other drugmakers for similar misdeeds.

In response to the ongoing investigation, the China Food and Drug Administration proposed revisions to its regulations and penalties related to inspections and investigations (see story, page 5). The CFDA gained added regulatory muscle last year, being elevated to ministry level in March of 2013.
Brazil also took aim at corporate bribery. President Dilma Rousseff signed into law legislation to stem bribery of government officials across all business sectors — bringing the country’s antibribery policies in line with other major nations and the Organization for Economic Cooperation and Development’s Antibribery Convention.

Drugmakers found guilty of offering bribes in Brazil, or abroad, may be fined up to 20 percent of their gross annual revenue from the previous year, up to about US $30 million. The law also gives the government the authority to suspend or dissolve a company’s operations and confiscate assets. Experts say companies that cooperate with officials can expect leniency regarding fines, and those with robust compliance programs and self-auditing procedures may see fines reduced by as much as two-thirds.

**U.S. Passes Track-and-Trace Legislation.** President Barack Obama signed the Drug Quality and Security Act into law on Nov. 29, capping a long-sought goal to create national track-and-trace requirements for prescription drugs. The law, intended to help prevent counterfeiting and drug diversion, immediately preempted all state laws concerning track and trace, including California’s strict e-Pedigree measure set to go into effect in 2015.

By Jan. 1, 2015, when the law takes effect, all finished dose forms of prescription drugs must include a lot-level transaction history that documents each step a product takes from manufacturer to final sale. Four years after enactment, drugmakers must affix product identifiers to each package and case of a product. The product identifier must include a numerical identifier, the drug’s lot number and the expiration date.

Also starting four years after enactment, manufacturers that intend to redistribute a returned product must verify the product identifier on each package. By 2025, companies must have an electronic traceability system that identifies products down to the sales-unit level. — Nick Otto

**Bribery ‘Blacklist’ is Latest Fallout From Ongoing GSK China Scandal**

Beginning March 1, China’s National Health and Family Planning Commission will publish a blacklist of drugmakers accused by provincial officials of offering bribes to customers. The blacklisted companies will be barred from selling their products for two years — four if it is a repeat offense.

The “Establishing commercial bribery record in drug/device purchase and sales” rule, issued Dec. 27, updates a 2007 rule on commercial bribery. The blacklist is the latest fallout from last summer’s drug bribery scandal involving GlaxoSmithKline. In September, the China Food and Drug Administration released proposed revisions to its regulations and penalties related to inspections and investigations (*IPRM, October 2013*).

The NHFPC rule also follows the 2012 launch of a blacklist for companies that knowingly market unsafe drugs (*IPRM, October 2012*). That initiative was sparked by revelations that some 13 percent of drug capsule makers in China were producing products with excessive, unsafe levels of chromium.

Drugmakers found guilty of bribery will have the records of their misdeeds published on the provincial NHFPC website. Within a month, they must be forwarded to the national NHFPC, which will also post them, explains Juliet Zhu, with L.E.K. Consulting’s Shanghai office. Bribery records include information such as company name, address, legal representative, name, title, incident and verdict.

Public or government-funded healthcare facilities that accept bribes will not be allowed to purchase products from the offending company for two years in the province where the offense occurred, Zhu says. Companies found guilty of bribery twice in five years will be barred from selling their products to publicly funded hospitals and clinics nationwide for an additional two years.

The rule also requires drug sales representatives and their clients to sign an “integrity sales contract,” committing to ethical and legal business practices.

The rule follows the Dec. 26 publication of a code of conduct on physician interactions with sales reps. Among other things, the code prohibits doctors from participating in promotional activities and accepting industry kickbacks.

Zhu likens the code to a “moral guidance” for physicians. Combined with the updated bribery rule, it underscores an “escalating” government commitment to stamp out graft and other illegal business practices, she says. — Nick Otto

**EMA Database Now Listing Names Of Noncompliant Manufacturers**

To discourage GMP scofflaws, the European Medicines Agency is now publicly naming drugmakers that aren’t in line with current good manufacturing practices.

The agency’s updated EudraGMP database includes, among other changes, the publication of statements of
GMP noncompliance. The statements contain information on the nature of the infraction and the actions taken, or proposed, by the issuing authority. As of Dec. 18, when the revised database was launched, 83 reports had been posted — the majority of them from Chinese and Indian manufacturers.

EudraGMP has provided public access to information on GMP compliance, import authorization, active pharmaceutical ingredient registration and other vital manufacturing information since 2011.

Naming GMP violators “fits in the larger policy of increased transparency that the EMA is pursuing across the board, as well as helps to make member state enforcement easier,” Erik Vollebregt of Axon Lawyers in the Netherlands tells *IPRM*. — Nick Otto

**Report Urges World Regulators to Act With Restraint on Opioid Restrictions**

The World Health Organization and advocacy groups from around the world are calling on drug regulators to ease “excessive regulatory restrictions” on opioid painkillers, saying they leave millions of cancer patients without effective pain management.

According to the report’s authors, excessive regulatory restrictions aimed at deterring drug abuse are to blame for an emerging “cancer pain pandemic” that affects more than half the world’s population. They are urging regulators to act with restraint before adding more restrictions to painkillers.

The report by the Global Opioid Policy Initiative — a collaboration of WHO and 19 international advocacy groups — recommends that opioids not be restricted to only patients with severe pain, but made available to patients with moderate pain as well.

Touted as the largest and most comprehensive review of opioid availability, the report covers 104 countries in Africa, Asia, Latin America, the Caribbean and Middle East, and parts of India.

The GOPI data highlight a wide range of issues that hamper availability, such as government restrictions and cost. Most countries in the Middle East, for example, tightly restrict access to opioid analgesics, requiring patients to register with government authorities, the report says. In certain Indian states, patients are required to obtain duplicate or triplicate prescriptions to access opioid drugs.

The review — which focuses on access to codeine, oral oxycodone, immediate and slow-release oral morphine, injectable morphine, transdermal fentanyl and oral methadone — comes as WHO is considering new restrictions on 26 popular painkillers, including widely used tramadol and tapentadol.

The U.S. Food and Drug Administration, meanwhile, has acted against recommendations such as those made by GOPI. In September, the agency announced that extended release/long-acting opioids would no longer be indicated for moderate pain and ordered labeling updates be made to all ER/LA opioid products.

The following month, the agency urged the Department of Health and Human Services to place hydrocodone combination products in a higher regulatory schedule to restrict access and encourage more cautious prescribing.

The GOPI study was published in the December issue of the *Annals of Oncology*. — Melissa Winn

**China to Pharma: Stop Foot-Dragging On New Vaccine GMP Certificates**

In the wake of a rash of infant deaths related to GMP-certified hepatitis B vaccines, China is renewing its push to have makers of vaccines, blood products and sterile injectables obtain a revised good manufacturing practice certificate.

The China Food and Drug Administration warned late last month that manufacturers that don’t get the new certificate will lose their marketing privileges. News of the vaccine-related infant deaths broke in November.

As of Jan. 1, 796 sterile drug manufacturers — about 60 percent of the total operating in China — had not met the new GMP requirements, according to the CFDA.

The agency expects all companies affected by the regulation, mandated in 2010, to comply before the end of the year.

Among other changes, the new rules establish a clearer quality management system and more detailed organizational structure, including responsibilities, procedures and resources to implement GMP activities, and specific qualifications for GMP personnel. Requirements for reporting and documentation, and for storage and production facilities, also are beefed up. — Nick Otto
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India Takes Steps to Control Flood Of Unapproved FDC Products

An advisory panel to India’s Central Drugs Standard Control Organization is calling for guidelines on the verification of fixed-dose combination drug products that are currently being sold without marketing authorization.

Since giving manufacturers 18 months to provide proof of safety and efficacy of FDCs or face market withdrawal, as many as 5,000 applications have been submitted to CDSCO, according to minutes of the agency’s Drugs Technical Advisory Board. Of those, many were found to have little or no therapeutic benefit, the committee says.

“In view of this, permission to market these FDCs were [sic] not granted. These FDCs are, however, considered to be available in the market as these appear in the monthly indexes of medical specialties,” the Nov. 27 minutes state. “In view of the large number of the applications, guidelines and procedures are required to be prepared for the examination of the FDCs.”

The DTAB suggested that a subcommittee be created to develop guidelines and make recommendations on examining and acting on those outstanding FDC applications.

The agency released a guideline last fall on the general approval of FDCs, which are regulated in India as new drugs. The guideline creates four FDC categories and provides information drugmakers and importers should include in premarket applications (IPRM, October 2013).

The parliamentary Standing Committee on Health and Family Welfare first drew attention to the issue of unauthorized FDCs in a scathing report in May 2012 (IPRM, May 2012). Among other concerns, the report found that 33 new drugs were approved between 2008 and 2010 without undergoing clinical trials. The committee cited a “collusive nexus between drugmakers, some functionaries of CDSCO and medical experts.” — Nick Otto

Foreign Direct Investment in India Gets Reprieve, But With Conditions

Foreign pharma can continue to invest directly in existing Indian drug companies, provided there is no “noncompete” clause in the transaction, the government says. The decision follows a call last summer for a total ban on foreign direct “brownfield” investments.

With the noncompete clause in place, domestic companies selling their facilities or operations to foreign investors cannot be barred from creating a fresh venture in the same therapeutic area.

The Jan. 8 notice from the Department of Industrial Policy and Promotion addresses concerns raised by the Indian Parliament’s commerce committee that foreign drugmakers were taking over legacy Indian companies. According to a committee report, only one of 67 FDIs in domestic pharma made through September 2011 was a “greenfield,” or fresh, investment (IPRM, September 2013).

Amy Hariani, director and legal policy counsel for life sciences at the U.S.-India Business Council welcomes the government’s decision to keep FDI in brownfield pharmaceuticals open, but worries about policy backsliding and the ramifications of protectionism if noncompetition agreements in brownfield investments are prohibited.

“Such measures would send a chilling signal to investors, chase capital to other markets and negatively impact the valuation and ability for domestic companies to grow and collaborate,” she tells IPRM.

The prospect of a ban on brownfield investments, coupled with recent court decisions favoring local generic drugmakers over foreign brand name competitors and new regulatory controls on clinical trials, has had foreign companies rethinking their presence in India. Whether the noncompete clause will discourage future investment, which India needs, remains to be seen, Hariani said. — Nick Otto

EC Pilot to Test Benefits of Early Talks Between Drugmakers, HTAs

The European Commission is looking for drugmakers to participate in pilots on early dialogue with health technology assessors, with the aim of better aligning new product development and HTA requirements.

The pilots — to be conducted by the Shaping European Dialogues, or SEED, Consortium under a Commission contract — will initially involve seven novel drugs. Three of the seven will involve face-to-face meetings with the European Medicines Agency and multiple HTAs. The other four will involve only HTAs.

Six to seven HTA bodies will participate in each multi-HTA early dialogue. The pilots are scheduled to begin in March and run through January 2015.

During the pilots, HTAs and companies will engage in discussions to “identify specific HTA needs related to
the relative effectiveness and cost-effectiveness assessment, notably to patient population and type of evidence needed (design of trials, duration, type of evidence endpoints, comparators),” a Dec. 22 call for interest states.

Drugmakers will get nonbinding advice on product development, while learning of different HTA and regulatory requirements across the EU. The goal is “to help design a robust global development programme,” the document says. Drug candidates should be pre-Phase III.

The SEED Consortium comprises 14 national and regional HTA entities led by France’s Haute Autorité de Santé. Funding for the pilot is authorized in the EU Health Programme 2008-2013.

The pilots echo U.S. efforts to encourage early dialogue between medtech developers, the U.S. Food and Drug Administration and Centers for Medicare & Medicaid Services, which determines which new technologies the government funds. Last month, the agencies extended for two more years a parallel review pilot for devices, saying they need more time to evaluate the program’s effectiveness.

The Commission’s call for interest will remain open until October. Applications received after the 10 candidates are selected may be considered for a reserve list in the event one of the participants halts product development, SEED says.

View the notice at www.fdanews.com/ext/resources/files/01/01-14-SEED.pdf. — Meg Bryant

EU Pay-for-Delay Agreements Decline Drastically in 2012

While the number of patent settlements between brand and generic drugmakers has risen in the EU for the fifth straight year, the number of agreements leading to pay-for-delay deals has dropped significantly.

In a report released Dec. 9, the European Commission says 183 patent settlements between brand and generic drugmakers were concluded in 2012, compared with 120 the previous year. Yet pay-for-delay deals, in which brand companies compensate their generic competitors for delaying market entry, accounted for only 7 percent of 2012 settlements, down from 22 percent of settlements reported between 2000 and the first half of 2008.

Commission Vice President Joaquín Almunia called the report a victory for all stakeholders. It illustrates that drugmakers are shying away from such anticompetitive deals, but are still able to amicably settle some disputes without drawn-out court battles, he said.

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The EU has been cracking down on pay-for-delay agreements in the pharmaceutical sector, most recently fining Novartis and Johnson & Johnson $22 million for delaying market entry in the Netherlands of a generic fentanyl patch, a painkiller used by cancer patients.

In announcing the fine Dec. 10, Almunia warned drugmakers to “think twice before engaging into such anticompetitive practices, which harm both patients and taxpayers.”

In June, the Commission fined H. Lundbeck A/S nearly $126 million and levied fines totaling $70 million on four of its generic rivals for their respective roles in 2002 pay-for-delay settlement deals tied to the Danish drugmaker’s antidepressant citalopram (IPRM, July 10). The four generic companies were India’s Ranbaxy; Alpharma, now part of Zoetis; Merck KGaA/Generics UK, the latter now part of Mylan; and Arrow, now part of Actavis.

The Commission said Dec. 10 it is also investigating Servier and other pharma companies for potentially delaying the market entry of generic perindopril, a cardiovascular drug, and an agreement between Cephalon and Teva that possibly delayed the entry of generic modafinil, a medicine for sleeping disorders.


— Melissa Winn

**French Watchdog Raps Merck Unit For Generic Delaying Tactics**

French authorities in December fined Merck US $21.5 million for attempting to stall market entry of generic versions of its opioid-dependence drug Subutex.

L’Autorité de la Concurrence accused Schering-Plough, now owned by Merck, of launching a predatory strategy in 2006 to thwart anticipated copycats of Subutex (buprenorphine). The strategy involved sending statements to physicians and pharmacists denigrating the bioequivalence and safety of the competing products, the agency said.

According to the agency, the communications highlighted differences in appearance, dissolution and excipients between the originator and the generic to dissuade the use of competitors’ products. For example, between February and May of 2006, Schering-Plough organized seminars and conference calls to pharmaceutical sales representatives to disseminate risks when prescribing the generic, even though the drugmaker had no justifiable proof of such studies, the agency says.

The drugmaker also offered significant discounts and kickbacks to pharmacists to continue use of the brand drug.

The campaign had the desired effect of reducing generic substitution, which impacted public reimbursement accounts by several million euros per year, according to the competition agency.

Merck said Thursday it has no plans to contest the allegations and promised to prevent future infractions of French competition law. The company also promised to retrain its marketing staff.

Earlier this year, French drugmaker Sanofi-Aventis was fined $52.6 million by l’Autorité de la Concurrence for marketing practices that discouraged sales of generic versions of the company’s blood thinner Plavix (clopidogrel). — Nick Otto

**UK Lawmakers Want More Sunshine On Trial Data, Point to Tamiflu**

Doctors and researchers should have full access to clinical trial data on products licensed in the UK to ensure that the cost-benefits, as well as safety and efficacy, are considered in prescribing and coverage decisions, lawmakers say.

“The Department [of Health] and the [Medicines and Healthcare products Regulatory Agency] should ensure, both prospectively and retrospectively, that clinical trials are registered on an appropriate registry and that the full methods and results of all trials should be available for wider independent scrutiny, beyond the work undertaken by regulators during the licensing process,” according to a Jan. 3 report by Parliament’s Public Accounts Committee.

The committee also calls for clear and frequent auditing of how much trial information is available and how much has been withheld. The report echoes a similar push in the EU.

The report stems from hearings last summer on access to clinical trial information and the government’s stockpiling of Tamiflu. The National Health Service spent upwards of US $696 million to ensure availability of the influenza drug, but had to write off about $122 million due to poor recordkeeping on how the drug was stored during the 2009 flu pandemic.
The committee said it was surprised and concerned to discover that information is routinely withheld about the methods and results of trials on treatments prescribed in the UK, pointing to Tamiflu (oseltamivir) as a key example.

“There remains a lack of consensus over how well Tamiflu works and there is disagreement about whether regulators and [the National Institute of health and Care Excellence] received all the information on Tamiflu during the licensing process,” the report states.

During the hearings, the MHRA expressed confidence that the European Medicines Agency had all the evidence on Tamiflu; however, the Cochrane Collaboration, a drug information advocacy group, concluded the EMA’s information was incomplete, the report says.

Last year, Roche said it was open to providing Cochrane’s reviewers access to clinical study reports for all 74 Roche-sponsored trials of Tamiflu. Researchers have lobbied since 2009 for the Swiss drugmaker to hand over all its clinical trial data on the drug (IPRM, December 2013).

In its defense, the company points out that Tamiflu has been approved in more than 80 countries and used by more than 95 million patients. The committee says the MHRA and NICE should consider reviewing their position on Tamiflu’s efficacy once the Cochrane review is complete.

“Cultural Blind Spot”

In the grand scheme, “Tamiflu is just one small microcosm,” Ben Goldacre, a transparency advocate and research fellow at the London School of Hygiene and Tropical Medicine, testified last summer. In a 2010 review by the U.S. National Institutes of Health, only half of all completed trials for currently marketed drugs had been published, and trials with positive results were twice as likely as those with negative results to see the light of day. “This is a deeply ingrained cultural blind spot for medicine, but it is one we have known about since 1986,” he said.

Industry defended its record on data disclosure in the wake of the committee’s report. “It is misleading to suggest that the pharmaceutical industry routinely withholds clinical trial data from doctors and researchers,” said Bina Rawal, research, medical and innovation director at the Association of the British Pharmaceutical Industry. “We recognize that there is still work to be done and we are continuing on a journey to achieving greater clinical trial transparency,” he said. — Nick Otto

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Canada Clarifies Rx Drug Submission Requirements in Updated Guidance

Health Canada issued guidance last month clarifying how the agency’s several centers will collect and manage information and material submitted by sponsors of prescription drugs.

The updated guidance follows the June 2013 replacement of Schedule F of the Food and Drug Regulations — substances and ingredients that require a prescription to be purchased — with the Prescription Drug List and addresses the following processes:

- Filing and classification of information and material;
- Submission holds;
- Screening of information and material;
- Evaluation of submissions;
- Refiled submissions;
- Accessing submission information; and
- Fees.

The guidance directs drugmakers to specified departments for each type of submission, from new drug applications to periodic safety update reports.

If a submission won’t be reviewed by the target review date, the center director must notify the sponsor. Sponsors that wish to update their submission during this time must inform the center within 30 days from the date of the update notice, the guidance says. The sponsor will have 60 days from the date the center receives the request to submit the updated information.

Drugmakers may access information about their submissions via the Drug Submission Tracking System. Regulatory project managers have been assigned to each bureau to “streamline administrative processes and expedite drug submission review,” the guidance says. When questions arise, sponsors are asked to reach out to their respective contact within the regulatory affairs division.

View the entire guidance, which took effect Dec. 19, at www.fdanews.com/ext/resources/files/01/01-13-CanadianSubmissions.pdf. — Nick Otto

Guidance Eases Use of PERs In Basic Clinical Research

The Canadian government has released a draft guidance aimed at streamlining the approval process for basic clinical trials using positron-emitting radiopharmaceuticals, or PERs.

The Dec. 16 draft notes that use of PERs in basic clinical research “poses minimal health risks, provided certain criteria are met.” If finalized, it would supersede earlier guidance that was considered overly burdensome for sponsors wanting to sell or import PERs for that purpose in Canada.

The guidance applies to PERs used in basic human research — studies aimed at advancing scientific knowledge that are not intended to fulfill any immediate diagnostic or therapeutic purposes. Basic studies using PERs with a predefined safety profile in humans are exempt from the trial approval requirements, the draft says.

Applicants for basic studies using PERs must demonstrate that they meet a set of seven inclusion criteria. The application, along with site and research ethics board information, must be submitted to the Biologics and Genetic Therapies Directorate, which regulates radiopharmaceuticals. The directorate has 15 days to notify sponsors on the outcome of their applications. If additional information is required, sponsors have two days to submit it.

PERs help researchers detect chemical changes in the body and have become an important tool in the understanding of Alzheimer’s disease and development of drugs to detect beta amyloid plaque, among other uses.

Stakeholders have until Feb. 14 to comment on the draft guidance, which is at www.fdanews.com/ext/resources/files/12/12-17-13-HealthCanada.pdf. — Ferdous Al-Faruque

Aussie Regulator Streamlines Submission of AE Reports

Drugmakers can now submit adverse event reports to the Therapeutic Goods Administration via email using the international E2B standard alone — a move aimed at reducing manual data entry and duplicate handling of information.

The E2B standard is one of several electronic standards specified by the International Conference on Harmonisation. Data supplied in this format can be entered directly into the TGA’s adverse event database with minimal user interaction, the agency says.

Under the old system, about 50 percent of AERs annually involved also copying the information into Council for International Organizations of Medical
Sciences, or CIOMS, forms. Switching to E2B submissions only will streamline AE reporting and reduce the potential for errors, the TGA says.

The change brings Australia’s AE reporting system in line with other regulators such as the European Medicines Agency, U.S. Food and Drug Administration and Health Canada. Drugmakers currently transmitting individual case safety reports electronically to other regulatory authorities use the same E2B standard as that adopted by the TGA.

The TGA has set up a dedicated email address, e2b.reports@tga.gov.au, for sponsors to submit AERs using the E2B format. — Nick Otto

**IN BRIEF**

**Swissmedic Clarifies ‘Generics’ Policy**

Following discussions with drugmakers, Swissmedic has clarified its policy on “generic” drugs. In October, the agency announced it lacked the legislative framework to approve generics and would hence only authorize known active pharmaceutical ingredients (IPRM, November 2013). Effective Jan. 1, companies seeking authorization of drug products should declare whether it is a new active substance or a drug with known active compounds with or without innovation. If the application is for a known active compound without innovation, the filer should also indicate if it seeks to have the drug included on a list of products that are interchangeable. Additional information is available at www.swissmedic.ch.

**India Renews Call for Import Alerts**

The Drugs Controller General of India repeated a call for drugmakers to inform the DCGI “immediately” of any import alerts and restrictions imposed by regulators abroad. The original request came in June, but “despite several import alerts and restrictions imposed by international regulatory authorities, no such information has yet been brought to the notice of DCGI,” the office says. Companies are asked to submit alerts to the State Licensing Authority.

**HSA Gives Nod to Triclosan in Antibacterials**

Singapore’s Health Sciences Authority is supporting use of triclosan as an active ingredient used in antibacterial soaps, antiseptics and cosmetics. Current studies show no long-term risks for humans through daily exposure, the agency says, downplaying possible risks suggested by animal tests. The statement comes as the U.S. Food and Drug Administration is reviewing the safety and efficacy of triclosan.

**Peru Sets Rules for Stock Liquidation**

Drugmakers with products in Peru may request up to 12 months to liquidate stock that no longer meet the parameters of classification or coding updates, according to a revised regulation on the registration, control and pharmacovigilance of healthcare products. Applications must include the drug’s lot, identification and serial numbers; quantity; labeling and packaging materials, if applicable; monthly sales average; and an invoice preceding the update necessitating the change. View the regulation, in Spanish, at www.fdanews.com/ext/resources/files/01/01-06-14-PeruStock.pdf.

**Groups Align on Ethical Collaboration**

The International Federation of Pharmaceutical Manufacturers and Associations and four other global health-care groups have signed a Consensus Framework for Ethical Collaboration. Goals include putting patients first, promoting ethical research and innovation, ensuring independence and ethical conduct, and encouraging transparency and accountability. Besides IFPMA, the consignees are the International Alliance of Patients’ Organizations, International Council of Nurses, International Pharmaceutical Federation and World Medical Association.
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