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Final EMEA Guideline on Excipients Excludes Products in Development

The European Medicines Agency’s (EMA) final guideline on data submission requirements for excipients in marketing authorization applications does not apply to drug products currently in the clinical research stages of development.

Excipients are components of a drug compound other than the active ingredient. Examples include fillers, disintegrants, lubricants, antioxidants, preservatives, stabilizers and permeation enhancers.

The exemption was not included in the draft guideline released last year, although the EMA recommends that firms consider the principles in the guideline during the development stages of drug candidates.

In addition to the exemption for drugs in the clinical research stages of development, the EMA also removed the following recommendation from the final guideline: “For biological excipients

(See [Excipients](#), Page 2)

Pharmaceutical Industry Lags in Production Efficiency

The pharmaceutical industry lags behind the food and beverage industry in measures of production efficiencies, leaving significant room for firms to improve manufacturing operations, according to a study prepared by enterprise manufacturing software firm Informance International.

The study assessed 50 manufacturing lines in operation from January to June this year and concluded that equipment failures were a significant contributor to lost capacity. The most efficient pharmaceutical production lines have an overall equipment effectiveness of 39 percent versus an equipment effectiveness rating of 63 percent for the most efficient food and beverage production lines, Informance said.

(See [Production Efficiency](#), Page 4)

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of animal or human origin, the risk of transmitting adventitious agents should be considered and appropriate documentation submitted (e.g., method of preparation and control of tissues and body fluids used as starting materials).”

The section of the guideline concerning the use of antioxidants and antimicrobial preservatives was slightly modified from the draft version with the added recommendation that the concentration of such preservatives in pharmaceuticals should be at the lowest feasible level, the EMEA says.

In explaining that both antioxidants (used to improve the stability of medicines) and antimicrobial preservatives (used to prevent microbial proliferation) are usually harmful to living cells, the EMEA says that use of such agents should be avoided whenever possible, particularly in pediatric formulations.

“Where antioxidants are used during the manufacture of the medicinal product, the release limits should be justified by batch data or a sound justification has to be provided, if the proposed specifications do not include an identification test and a content determination test for the antioxidant. If needed, the adequacy of the specified limits should be justified on the basis of controlled conditions and (in-use) stability testing, to ensure that sufficient antioxidant remains,” the EMEA says.

Stability of Product

For determining the stability of finished pharmaceutical products, the content of the antimicrobial preservative should be monitored throughout the shelf life of the drug to ensure “the levels of preservative remain above the levels challenged for preservative efficacy and within the specifications,” the EMEA says.

However, when products are presented in multidose containers, the agency removed a suggestion that firms examine the efficacy of antimicrobial preservatives following storage in opened or used containers for the proposed in-use shelf life, although their efficacy must be established under simulated in-use conditions.

For assays covering excipients listed in the European Pharmacopoeia, or a pharmacopoeia of a European Union member state, it may be necessary to add tests and acceptance criteria to the pharmacopoeial specification, depending on the intended use of the substance, the EMEA says.

For excipients not described in any pharmacopoeia, the following types of tests should be used to establish their appropriate specifications:

- Physical characteristics;
- Identification tests;
- Purity tests, including limits for total and individual impurities, which should be named, e.g., by reference to a chromatographic relative retention time. Purity tests may be physical, chemical, biological and, if appropriate, immunological;
- Assay or limit tests, if necessary, and corresponding validation parameters; and
- Other relevant tests, e.g., tests on parameters (quantitative), which have been determined to influence the performance of the dosage form.

The guideline’s requirements for novel excipients, substances used for the first time in a drug or in a new route of administration, remained unchanged from the draft and the previous Eudralex 3AQ9a guideline on excipients.

In addition, when applying for authorization for a medicinal product, manufacturers should list excipients, their common name, amount, function and a reference to a relevant standard, the guideline says. Listings of excipients that include a mix of compounds should include a qualitative and quantitative breakdown of the substance, the guideline says.

The new guideline, “Excipients in the Dossier for Application for Marketing Authorisation of a Medicinal Product,” takes effect in January 2008 and replaces the previous Eudralex 3AQ9a guideline, as well as the “Note for Guidance on Inclusion of Antioxidants and Antimicrobial Preservatives in Medicinal Products.”

The guideline can be accessed at www.emea.europa.eu/pdfs/human/qwp/39695106/enfin.pdf. — Christopher Hollis, Meg Bryant

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Production Efficiency, from Page 1

“There is a large gap in performance in pharmaceutical operations that has huge upside potential for reducing operational costs and, where appropriate, improving capacity for those products that they can’t produce enough,” John Oskin, executive vice president of Informance, told *DGR*.

When comparing different drug manufacturing lines, the most efficient firms had a loss of 7 percent of capacity due to equipment failures, while the least efficient firms experienced a loss of 26 percent of capacity due to failures, according to the study.

In addition, cycle erosion, a measure of performance loss from minor stops, hesitations, reduced speed and operator fatigue, was 9.5 percent for the most efficient drug firms, while the most efficient food and beverage companies only had a 3.2 percent cycle erosion rate.

Despite the different regulatory environments for the respective industries, there is still room for improving production efficiency within the drug industry, Oskin said.

“There are definitely restrictions that make it more difficult to drive improvements in pharmaceutical operations, but the manufacturing challenges are the same,” Oskin said. “High volume operations, frequent changeovers, smaller lot sizes, these are themes that apply whether you are talking about pharmaceutical or food and beverage.”

Oskin agreed that drug firms historically could afford less-efficient production operations because they have higher profit margins than the food and beverage industry. However, drug companies are increasingly focused on improving manufacturing operations as generic competition for several large product franchises puts cost pressures on manufacturing and corporate operations, he explained.

“The competitive cost pressures today just weren’t there five years ago,” Oskin said. “In the past two or three years ... we’ve noticed a significant increase in the focus on operational excellence.”

Many of the production inefficiencies observed by Informance were logistical in nature. “It’s not about the machine breaking down, per

se, it’s the fact that changeover took twice as long as it should, the fact that somebody slowed down the machine for some reason because of an incoming vendor quality problem with materials. Because in their batch operation, where they’re actually producing the drug, the product is not actually making it to the packaging area, and so the lines are starved of product.”

Oskin recommended that companies constantly measure production operations with key performance indicators (KPIs) and institute processes to react quickly to KPIs that deviate from acceptable levels. — Christopher Hollis

Novartis, Sanofi Start Shipping Flu Vaccines to U.S.

Novartis and sanofi pasteur, the vaccines division of sanofi-aventis, have begun shipping their influenza vaccines, Fluvirin and Fluzone, to the U.S. for the 2007-2008 flu season, the companies announced last month.

Novartis plans to ship approximately 40 million doses of Fluvirin to the U.S. for the upcoming season, of which nearly 7 million have already been made available. Sanofi pasteur said it has begun shipping the first of the 50 million doses of its vaccine Fluzone under a partial shipment delivery program. Orders for sanofi’s vaccine are expected to be filled by October.

Furthermore, Novartis anticipates delivering at least 20 million doses by the end of September, with all doses expected to be sent by the end of October. The first lots of Fluvirin vaccine were released Aug. 8, making it the first trivalent inactivated influenza vaccine available this season, the company added.

Sanofi said it produces “approximately half of the influenza vaccine distributed worldwide and more than 40 percent of influenza vaccine distributed in the U.S.”

As of Aug. 21, the FDA said it released 32 lots of Fluzone, 17 lots of Fluvirin and five lots of GlaxoSmithKline’s flu vaccine Fluarix. — Breda Lund, Martin Gidron

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Dingell Introduces Draft Legislation To Increase Import Inspections

Early last month, Rep. John Dingell (D-Mich.) introduced draft legislation that would establish a user fee on imported drug shipments to fund more inspectors at the U.S. border and in FDA laboratories.

The user fees would be used to test samples of drug imports and research new testing techniques, according to an announcement from the House Energy and Commerce Committee, which Dingell chairs. The bill would also create a similar user fee and new programs for imported food products.

The greatest priority for using the fees would be for inspections and testing to detect intentional adulteration or misbranding of drugs, according to the committee.

In addition, the bill would give the FDA the authority to call for mandatory recalls, and would increase civil monetary penalties for manufacturers and importers who do not comply with the Food, Drug and Cosmetic Act. The civil monetary penalties would be raised to \$100,000 for an individual and \$500,000 for a company introducing or delivering a noncompliant product, with a maximum of \$1 million for all violations in a single proceeding, according to the committee.

The FDA's ability to conduct inspections and analyze laboratories is "declining," according to Dingell's announcement. The bill would bar the HHS secretary from closing or consolidating the 13 agency field laboratories.

FDA Commissioner Andrew von Eschenbach recently said he would delay reforms to the agency's Office of Regulatory Affairs until a working group completes its assessment of import safety (*DGR*, August).

HHS Secretary Michael Leavitt, chair of the Working Group on Import Safety, has decided to focus the group on imported drugs, medical devices and food, according to von Eschenbach. The group will issue a report with recommendations on how to ensure the safety of imported products shortly,

von Eschenbach said, adding that Leavitt has already begun a series of meetings.

After the group issues its report, the FDA plans to hire inspectors in a strategic way, focusing on where they should go, what they should inspect and what tools they need to be effective, von Eschenbach said.

The draft legislation can be viewed at [energycommerce.house.gov/China Food Safety/Food Safety Draft Bill.pdf](http://energycommerce.house.gov/China_Food_Safety/Food_Safety_Draft_Bill.pdf). — Emily Ethridge

Grassley Grills Von Eschenbach on Foreign Manufacturing Inspections

Sen. Chuck Grassley (R-Iowa) asked FDA Commissioner Andrew von Eschenbach to explain the agency's steps to ensure the safety of drugs made in foreign countries.

Grassley is "troubled" by reports of agency failures in inspecting foreign pharmaceutical manufacturing plants. Nearly 80 percent of active pharmaceutical ingredients are manufactured abroad, he said in a letter to sent von Eschenbach early last month.

In addition, Grassley asked for a formal response to questions on what protocols and specific steps the FDA takes when inspecting foreign facilities, as well as details of agency site visits to foreign facilities.

Grassley asked how much the agency spends on foreign investigations annually, how many inspections were for facilities manufacturing generic drugs, how long FDA inspectors stay abroad, and what follow-up occurs after a negative review.

Grassley also asked about the agency's cooperative relationships with other foreign regulatory bodies, and the adequacy of those agencies' facility inspections.

He asked how the FDA is preparing to respond to a possible large shift from domestic manufacturing facilities to facilities in Asia and if the agency has any plans to create an outpost in India. — Emily Ethridge

Amgen Laying Off up to 2,600 Employees Over Slow Aranesp Sales

Amgen announced that it is laying off 2,200 to 2,600 employees — 12 to 14 percent of its work force — cutting approximately \$1.9 billion in planned capital expenditures this year and next, and possibly closing or “rationalizing” some production facilities.

Amgen expects these and other “restructuring” steps to generate pretax savings of \$1 billion to \$1.3 billion next year. The company said it will attempt to soften the blow to laid-off workers by relying on attrition, hiring freezes and a voluntary transition program to achieve as many of the job cuts as possible, as well as giving career counseling to those who are pushed out.

The company said the restructuring is needed because of lower revenues from Aranesp (darbepoetin alfa), which is used to treat kidney disease-related and chemotherapy-induced anemia. This drug is part of a class of products called erythropoietin-stimulating agents (ESAs), that

have faced safety concerns recently, including Amgen’s Epogen (epoetin alfa). Earlier this year, the FDA added new warnings to physician labeling for the products, and the Centers for Medicare & Medicaid Services has instituted more restrictions for reimbursement of ESAs.

U.S. sales of Aranesp fell 18 percent to \$578 million in the second quarter of 2007, compared with the same period last year, although international sales of the product increased 8.5 percent to \$371 million.

The company said the restructuring would allow it to keep R&D spending high; however, it will be reevaluating various projects to decide which deserve the highest priority.

“Recent changes in coverage rules and adjustments to Amgen’s FDA-approved labels for Epogen and Aranesp have and will adversely affect Amgen’s revenue,” Kevin Sharer, Amgen chairman and CEO, said. “The initiatives announced today respond to that new reality by taking account of reduced revenues and appropriately lowering costs across the company.” — Martin Gidron

Valuable Information Will Likely Not Be Included in EudraGMP Database

The European Medicines Agency’s (EMA) new EudraGMP database will likely not include valuable information, according to Peter Smith, vice president of pharmaceutical compliance for Parexel Consulting.

The publicly available information in EudraGMP will likely “be very restricted and probably a lot of the information that’s available publicly will be purged of a lot of useful information,” Smith said during an FDAnews audioconference last month. “But at least this is a step toward making some of their information public, and we’ll just have to see how and when this actually comes to pass.”

The EMA announced the new database earlier this year and the FDA plans to use the system to prioritize inspections (*DGR, May*). The EMA plans to grant public access to EudraGMP for manufacturing and import authorizations and

“certain GMP certificates” by the end of the year, the European regulator said.

According to the EMA, other features planned for future releases of EudraGMP include information on noncompliance, inspection schedules in non-European countries and alerts for member states regarding GMP noncompliance, and suspension or revocation of manufacturing authorizations.

Smith also detailed the differences between FDA and EMA inspections.

EMA inspectors tend to have more industry experience, considering the relatively young age of FDA investigators, Smith said. For example, Swedish inspectors have an average of 10 years experience, while auditors from the UK’s Medicines and Healthcare products Regulatory Agency are required to have at least five years of industry experience as a prerequisite, Smith said.

(See [EMA Inspections](#), Page 8)

Discovery Labs Sees Resolution To Manufacturing Issues

Discovery Labs is anticipating approval for its preventative respiratory distress syndrome (RDS) drug Surfaxin in the spring of 2008 as it resolves manufacturing issues that have long-delayed approval of the product, the company announced last month.

Last year the FDA issued a second approvable letter for Surfaxin (lucinactant) that requested additional information regarding further tightening of active ingredient and drug product specifications (*DGR, May 2006*). Shortly after the second approvable letter, the firm said that process validation batches of Surfaxin failed stability tests. Three senior Discovery Labs executives left the firm shortly thereafter.

Surfaxin batches used during clinical trials are not in question, and the FDA has no issues regarding the efficacy of the product, Discovery Labs said.

Since the company switched contract manufacturers for the product from Akorn to Laureate Pharma, manufacturing issues have hampered production. The company purchased the contract manufacturing facility from Laureate in December 2005.

The FDA issued Form 483 inspection observations for the operation in 2005 and 2006. At the

time, the firm said the observations were related to quality controls, process assurances and documentation requirements, and that there were no fundamental flaws to the Surfaxin manufacturing process.

The company told *DGR* that some modifications to the production process were instituted during the change in manufacturing operations, which resulted in stability issues. The operation subsequently reverted to the original manufacturing specifications.

The firm completed the manufacture of three process validation batches in February. The batches have demonstrated acceptable stability over three months. The entire stability data package is expected to be submitted to the FDA in October, the company said.

Surfaxin is a synthetic surfactant. Currently marketed surfactants, such as Abbott Laboratories' Survanta (beractant), are derived from animals. — Christopher Hollis

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“The FDA tends to be more system and documentation focused, maybe spending more time in the conference room reviewing documentation, whereas the EMEA is more operations focused, and they may spend more time out in the lab or out in the plant,” Smith said. “Probably this comes from their industry experience. They feel comfortable out in the plant and so forth, whereas FDA feels a little bit more comfortable just reviewing documents.”

European inspectors also tend to be less strict about investigations for out-of-specification results, focusing on justifications and resolution of the problem, while the FDA tends to be more enforcement oriented, focusing on whether the investigation was properly resolved and what the product impact determinations were, Smith said.

Despite their differences, EMEA inspectors have tended to become more FDA-like in recent years, spending more time reviewing records, Smith said. Likewise, FDA investigators are increasing the time they spend observing facility operations during inspections. — Christopher Hollis

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European Commission Pulls Viracept Marketing Authorization

The European Commission officially suspended the marketing authorization for Roche's HIV treatment Viracept last month following a late-June recommendation from the European Medicines Agency (EMA).

"The suspension can only be lifted by a further decision of the commission, after an assessment by the agency of new data," the commission said.

The EMA recommended that the commission revoke Viracept's (nelfinavir mesylate) authorization following a firm-initiated recall of all batches produced for European consumption. Roche halted sales of the drug before the EMA's recommendation (*DGR*, July).

The recall was initiated in early June after product complaints said some batches of the product had a strange odor. Following a chemical analysis, Roche found the batches contained methanesulfonic acid ethyl ester, or ethyl methansulphonate (EMS), a substance believed to cause damage to DNA.

Report: Asia to Become Largest Pharmaceutical Market

As the global pharmaceutical market is shifting to Asia, companies are advised to establish a presence there to begin tackling the region's obstacles and keep up with the changing tide, according to a recent PricewaterhouseCoopers report.

The report found that competition among Asian countries to attract international pharmaceutical players is intensifying as governments offer various incentives. The results were based on a survey of 185 senior pharmaceutical executives from 92 domestic Asian companies, and 93 multinational companies with operations in nine different Asian countries, including China, India and Singapore.

Among the executives surveyed, one-third of multinational company executives said they have immediate plans to further expand in Asia through acquisitions or by development of newly

Roche told *DGR* that the root cause of the contamination has been confirmed, which was related to the cleaning process of a mixing tank, and that the company is anticipating submitting data on a revalidated production process to the EMA this fall.

The firm is still in supply discussions with Pfizer as another option to return Viracept to the market. Pfizer makes the drug for U.S., Canadian and Japanese consumption, while Roche manufactures the HIV treatment for European markets.

"Any drug purchased from Pfizer will need to meet the new [European Union] specification of less than 0.6 ppm of EMS in the finished batches. Since this is a new specification, Pfizer told us on Aug. 15 that they are in the process of testing for EMS at these levels. We are waiting for further word from Pfizer," Roche told *DGR*.

In late June, the EMA and Roche agreed to establish a registry to follow patients that were exposed to the contaminated product. The company has also agreed to conduct animal studies to more precisely calculate toxicity levels of the contaminant in humans, preliminary results for which will likely be submitted to the EMA by the end of this year. — Christopher Hollis

built sites, and 65 percent of Asian company executives said increased global market share is important for their companies.

Overall, the report predicts that Asia will become the biggest pharmaceutical market in the world. A presence in these markets — such as through outsourcing — gives multinational companies market knowledge and the opportunity to adjust to the environment.

So far, companies that outsource to Asia have been focusing primarily on outsourcing manufacturing, but companies are increasingly starting to outsource clinical trials, R&D and other activities, the report found.

The report, "Gearing Up for a Global Gravity Shift: Growth, Risk and Learning in the Asia Pharmaceutical Market," is available at [www.pwc.com/extweb/pwcpublishings.nsf/docid/76DEF9E310AB1DCD802572DF002C5ECA/\\$File/gearing-up-gravity.pdf](http://www.pwc.com/extweb/pwcpublishings.nsf/docid/76DEF9E310AB1DCD802572DF002C5ECA/$File/gearing-up-gravity.pdf). — Breda Lund

Communication Key to Compliance, Former FDA Counsel Says

Companies should be forthright in communicating with the FDA and bulk up their pharmacovigilance systems to comply with new enforcement tactics, former FDA Chief Counsel Daniel Troy said at the Third Annual FDA Regulatory and Compliance Symposium at Harvard University.

The agency's enforcement focus is shifting to a risk-based approach, as legislation pending in Congress could grant the FDA more postmarketing authority, Troy said. Companies should create strong internal monitoring controls and a culture of compliance and transparency to avoid enforcement actions, he added.

"There is absolutely no benefit to not telling FDA whatever you find out as quickly as possible," according to Troy.

Regular audits can be helpful, but a company must have a culture of compliance that it continually revisits. "You can't audit yourself into compliance," Troy said.

While the FDA's risk-based approach emphasizes internal controls and strong GMP protocols, Congress is pushing the other way and questioning the agency's enforcement actions, Troy said.

Rep. John Dingell (D-Mich.) recently sent the agency a letter investigating its handling of a warning letter related to Johnson & Johnson's Cypher stents. If sending warning letters contin-

ues to expose the agency to criticism, "we're going to see a big jump in precipitous and unnecessary action by FDA in the enforcement context," according to Troy.

Regardless of what and how much authority the FDA is granted in the final legislation, the enforcement trend will be toward having a robust pharmacovigilance system, Troy said. "Active surveillance and data mining is important in assuring the agency your product is worth approving," he said.

In addition, companies can use tools such as citizen petitions to communicate with the FDA about whether a practice is legal. Petitions can ask the FDA to clarify the issue through a guidance, put the company's position on record and show that the company is open and transparent, Troy said. Firms should also participate in public meetings to get involved in working with the agency, he added.

These moves can also help companies deal with nonscientific regulators, such as the Department of Justice, state attorneys general, Congress, the media, "so-called consumer groups" and medical journals, which are becoming increasingly politicized and have "nonscientific agendas," Troy said.

Since the FDA says it has preemption over state law challenges to labeling, plaintiffs' lawyers and state attorneys general are focusing on other company activity, Troy said. GMP, good clinical practices or good laboratory practices could be the next focus area for lawsuits, he added. — Emily Ethridge

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Computerized Audit Trails for Clinical Trials a Must

Although the FDA altered its recommendations in a recent guidance for audit trails of computer systems used in documenting clinical trial results, sponsors should still carefully consider how to comply with audit trail requirements under the agency's 21 CFR Part 11 regulation, according to former FDA official Stan Woollen.

The FDA issued its revised "Computerized Systems Used in Clinical Investigations" final guidance earlier this year.

"In the old guidance, it said you needed to have computer-generated, time-stamped audit trails, just as Part 11 does. But that's been minimized in" the new guidance document, Woollen, a senior compliance adviser with Woollen and Associates, said during an RxTrials Institute audioconference.

In the new guidance, the FDA is "basically saying that the need for audit trails is optional based on a justified document and risk assessment," Woollen said. However, "that's a pretty high risk area and you might want to consider carefully how you're going to comply with the audit trails [recommendations]."

When asked how stringently the FDA will enforce its recommendations that audit trails should document reasons for changes to clinical trial computer data, Woollen said that if the changes make subsequent

(See [Audit Trails](#), Page 2)

IBM Introduces ePedigree System

IBM announced the introduction of an ePedigree system that it said will help pharmaceutical companies combat drug counterfeiting and comply with regulations.

The ePedigree feature is a capability of the new version of IBM's WebSphere RFID Information Center (RFIDIC), a data repository allowing clients to manage and securely share information with trading partners to authenticate pharmaceuticals.

Pharmaceutical companies can create an ePedigree for every drug that passes through the supply chain, giving all supply-chain participants secure and on-demand access to data on individual bottles or packages of medicine, IBM said.

Unlike competing solutions, the IBM offering was designed to manage and aggregate product serial numbers to enable processes in manufacturing plants, distribution centers, pharmacies and hospitals, the company said.

The ePedigree feature allows clients to comply with new and emerging regulations, such as those that will take effect in California in 2009, using either radio frequency identification (RFID), 2D barcodes or a combination of barcodes and RFID.

(See [IBM](#), Page 2)

Audit Trails, *from Page 1*

clinical study reconstructions noninterpretable, then the FDA might take issue with the system, despite its not being a regulatory requirement.

“If I were doing an audit and I saw a pattern of changes that weren’t for one of the usual reasons, or that I couldn’t intuitively determine why this pattern of changes were being made, I would expect to see some kind of documentation in the record,” Woollen said. “I’d certainly ask the site personnel, [for example], ‘Why did you change all of the blood pressure data on the last five readings for these patients when they dropped out of the study?’”

In addition, although the FDA removed system validations from the recent guidance, Woollen suggested that firms should still send out specialized auditors to check if vendors’ electronic data capture systems are validated.

According to Woollen, the FDA is giving companies more flexibility in the guidance, saying that decisions for validation audits can be made through risk assessments.

“Frankly, the policy leaves a lot of things up in the air and kind of waffling. I think the agency itself is waffling on the issue. But what their approach has been is to essentially say that, ‘It’s up to you, you can decide, for example, what systems that you think need validation and how you’re going to go about doing that,’” Woollen said.

However, validation requirements under Part 11 are still enforceable, although the FDA said it would essentially look the other way until the regulation is finalized. “I wouldn’t take that as any sort of signal to say that ... we no longer need to focus on validation,” Woollen said.

The most difficult aspects of Part 11 that manufacturers have to contend with are the areas where the FDA said it would use enforcement discretion, meaning it would not recommend enforcement actions for violations that were identified in its final guidance on Part 11 electronic records issued in 2003, Woollen said.

These areas include legacy systems — systems that were in place before Aug. 20, 1997 — which lead to problems associated with audit trails and validation. Those problems can be associated with new systems as well.

In addition, Woollen said firms need computer system disaster recovery plans. Although FDA regulations do not specifically require that clinical trial computer systems have such plans, if data from the system are lost, the FDA could cite the company for failing to maintain adequate records.

Further, the clarity of data entry fields and forms, as they were programmed when the system was first designed, should be taken into account when trying to employ a system that minimizes errors, Woollen said.

The audioconference, “New Part 11 Guidance for Clinical Trials: What This Means for You,” can be accessed at www.fdanews.com/conference/detail?eventId=964. — Christopher Hollis

IBM, *from Page 1*

Also new are enhanced reporting tools and alerting capabilities, IBM said. The reporting feature allows clients to access and analyze data using browser-based reports for faster decisionmaking. The report data can be used for numerous business needs, such as reverse logistics and inventory management. Through the new alerting feature, businesses can rapidly detect supply chain exceptions, such as a late shipment, and generate alerts to the appropriate personnel.

For additional flexibility, customers using the new version of WebSphere RFIDIC can set up rules for how their supply chains should work and what should happen if an exception to these rules occurs, IBM said.

AmerisourceBergen is already using WebSphere RFIDIC in its Sacramento pilot with a large global pharmaceutical manufacturer, the company said. It added that it is working with its customers in the pharmaceutical industry to enhance the product’s capabilities. — Martin Gidron

Billions Will Be Spent on EDC, Study Says

The pharma industry will spend a total of more than \$3.1 billion on electronic data capture (EDC) between 2006 and 2011, according to a new report by Health Industry Insights. In 2009 alone, spending on EDC in Phase I, II and III trials will total \$508 million, compared with \$302 million last year. The compound annual growth rate of spending on EDC will be 14.7 percent between 2006 and 2011, the study said.

Moreover, “2007 will mark a tipping point,” as the rate of growth of EDC adoption rises from 6.5 percent to 13.3 percent, the study said. By the end of 2007, 45 percent of all new Phase I to III studies will use EDC, the study’s authors predicted.

The study offers several suggestions for companies buying EDC systems:

- Invest in “considerable cultural and process re-engineering” of existing clinical development processes to get the most out of EDC;
- Sponsors should require EDC vendors to “invest in the appropriate support staff” to help “technically naïve users speaking different languages in different cultures and in different time zones” at sites; and
- “Look for EDC vendors that can provide a common platform to integrate multiple sources of clinical data.”

For their part, EDC vendors should expect sponsors to institute “increasingly rigorous requirements” for such matters as service outages and disaster recovery, the report said. “Accordingly, EDC vendors should increase the reliability of their hosted services without increasing the hosting fee to their customers.” Vendors should also be prepared to offer increased flexibility; data encryption and other security technologies; lower pricing models and subscription-based services; self-service and user-focused toolkits; and appropriate support staff.

The report is available online at www.health-industry-insights.com. — Martin Gidron

FDA, DoD to Share Data on Medical Product Safety

The FDA and the Department of Defense (DoD) have signed a memorandum of understanding in which they have agreed to share data and expertise in reviewing the safety of medical products, with the latter contributing data from the U.S. Military Health System.

The agencies said the first data the DoD shares would most likely be prescription information from Tricare, the agency that administers the healthcare plan for 9.1 million members of the uniformed services, retirees and their families.

The FDA said it would use the Tricare prescription information and other general patient data, such as lab results and patient weights, to spot trends that could be worrying or potentially beneficial. The FDA and the DoD emphasized that they will protect all personal health information exchanged under the agreement, in accordance with federal law.

The data will be integrated into the FDA’s Sentinel Network, an initiative first announced in January that is intended to explore the possibility of linking private- and public-sector medical product safety information into a virtual, integrated electronic network. This could eventually include new medical product information, patient care records, adverse event reports, and information on domestic and international clinical trials, among other things.

“Currently, most drug studies performed prior to FDA approval involve about 1,000 patients, and follow-up studies use similar numbers,” Assistant Secretary of Defense for Health Affairs S. Ward Casscells, who signed the memorandum of understanding on behalf of the DoD, said.

The DoD and the FDA will meet later this year to establish specific procedures and safeguards. The memorandum of understanding can be accessed at www.fda.gov/oc/mous/domestic/FDA-DOD-INFO.html. — Martin Gidron

BRIEFS

Electronic Data Archiving Document

ISPE announced the release of its technical publication, "GAMP Good Practice Guide: Electronic Data Archiving."

According to ISPE, the guide provides a "rational and scaleable approach" to electronic data archiving through the development of an archiving strategy. It addresses management, planning, development, and operational and compliance issues, ISPE said.

The guide gives companies an introduction to the subject of electronic data archiving, recognizing the differences from the traditional paper archive, ISPE said. It provides a process for creating and implementing an archiving strategy and identifies aspects of technology that affect the selection of an archive solution.

The guide also addresses the "fundamental role" of the archiving strategy document, ISPE said, adding that archiving regulations have been taken into account in developing the guide.

SYSPRO Compliance Software Enhanced

SYSPRO announced significant enhancements to its SYSPRO CRM (customer relationship management) solution that it said will enable manufacturers to "more easily comply with FDA regulations."

Among the new enhancements are the easier recognition of inactive accounts and contacts, and the use of SQL Optimization to speed up record

searches. In addition, the integration of SYSPRO CRM with Microsoft MapPoint allows authorized users to display maps of accounts and contacts in the U.S. and Canada, pinpointing geographical areas where tainted or defective product may have been shipped, SYSPRO said. This feature may aid in future marketing and sales strategies as well, it said.

Further, the availability of HTML formatting for activity notes presents SYSPRO CRM users with new options to accommodate FDA reporting requirements, the company said.

E-WorkBook Validated for FDA Regs

IDBS, an electronic laboratory notebook (ELN) provider, announced that its E-WorkBook Suite has been independently validated by the Sociedad de Validacion de Sistemas (SVS) against the FDA's 21 CFR Part 11 and Good Laboratory Practice Guidelines.

SVS, a Spain-based validation and compliance consulting company, serves the pharmaceutical industry in various technical fields. According to IDBS, its full E-WorkBook Suite, which includes its BioBook and ChemBook, has been successfully validated. The individual workbook has been validated since 2006.

The full workbook suite provides a framework for laboratory studies to be performed, monitored, recorded, reported and archived. Its audit trail meets the FDA's electronic document rules.

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