In the wake of the global recession, governments across the world spent 2010 working toward recovery using the pharmaceutical industry as an area to cut costs through pricing reforms, but at the same time, issued guidances that aim to bring cheaper drugs to market and took a harder line on company malfeasance.

Two Canadian provinces instituted pricing reforms that cut generic drug costs. In June, Ontario approved regulations to reduce the cost of generic drugs to 25 percent of the cost of the original brand-name drug (IPRM, June 2010). Following in Ontario’s footsteps, British Columbia will slash generic drug prices to 35 percent of the brand price over the next three years (IPRM, July 2010).

Meanwhile, the UK proposed a value-based pricing system for drugs that would establish a new model for pricing and reform the National Institute for Health and Clinical Excellence (NICE), which evaluates the cost-effectiveness of drugs and medical technologies (IPRM, June 2010). In mid-December, the Department of Health released for consultation its plan for the value-based pricing system, accepting comments until March 17 (see story, page 7).

In December, Ireland also began publishing guidelines on the cost-effectiveness of healthcare technologies (IPRM, December 2010).

Germany also joined the trend with Health Minister Philipp Rosler proposing a price restructuring that would require drugmakers to prove a new drug has a superior cost-benefit ratio compared with existing treatments as a basis for price negotiations with public health insurers (IPRM, December 2010). Since Germany is a reference country, its pharmaceutical price control legislation may lead to similar legislation in other European countries (IPRM, December 2010).

Australia also worked toward drug pricing reforms, initiated through a memorandum of understanding between the country’s pharma industry and the government that combined new drug price reductions with the promise of a stable economic environment for research and development in the future (IPRM, May 2010).

While pricing reforms grabbed many headlines, other developments in 2010 sought to increase innovation and help consumers. One such area was the increasing importance given to follow-on biologics...
and the scramble by many governments to create guidance related to their development.

Health Canada began in March with a draft guidance requiring that manufacturers who submit a new drug application for a subsequent entry biologic provide extensive scientific evidence of similarity with the reference biologic (IPRM, March 2010).

The U.S. Food and Drug Administration (FDA) followed suit one month later with a rule amending its biologic constituent regulations, allowing it to approve exceptions or alternatives if companies demonstrate the safety, purity and potency of a biological product (IPRM, April 2010). The agency then urged manufacturers to be patient while it creates a new regulatory framework (IPRM, July 2010).

In November, the FDA held its first public meeting on a pathway to approval for biosimilars, answering industry questions and requesting opinions on the topic (IPRM, October 2010).

The UK also weighed in on follow-on biologics with the National Institute for Health and Clinical Excellence recommending approval of its first biosimilar, Sandoz’s Omnitrope (somatropin), which is comparable to Pfizer’s Genotropin, for treatment of child growth deficiencies (IPRM, June 2010).

For new biologics, the Australian House of Representatives approved legislation that would create requirements as part of a biologic-specific regulatory framework (IPRM, May 2010). At the end of the year, the country made amendments to its Therapeutic Goods Regulations from 1990 creating a new regulatory framework for biologics that drug manufacturers must abide by following implementation this year (IPRM, December 2010).

**Year of Investigations**

While pharmaceutical companies focused on developing new treatments, regulators spent much of the past year delving into allegations of industry transgressions.

Continuing ongoing investigations into pay-for-delay cases, the European Commission (EC) kicked off 2010 by targeting Danish drugmaker H. Lundbeck, who the EC investigated in regards to delaying a generic version of its antidepressant Cipramil (citalopram hydrobromide), known as Celexa in the U.S. (IPRM, January 2010).

In July, the EC reported a decline in potentially problematic patent settlements claiming the sharp drop was due to ongoing antitrust investigations (IPRM, July 2010).

Australia joined the fray and fined drugmakers for misleading claims and breaching code of conduct. Roche allegedly made misleading claims about its anemia drug Micrera (methoxy polyethylene glycol-epoetin beta) and was fined $200,000. AstraZeneca was fined $75,000 for promoting prescription-only Nexium (esomeprazole magnesium) for heartburn relief to the general public, and a $15,000 fine related to hospitality at an educational event. Other companies fined for code violations included Janssen-Cilag, Sanofi-Aventis and Alcon Laboratories Australia (IPRM, November 2010).

Meanwhile, the U.S. Justice Department and the U.S. Securities and Exchange Commission instituted investigations into illegal payments to foreign officials under that nation’s Foreign Corrupt Practices Act (FCPA). Violations focused on offering kickbacks in exchange for favorable actions on a drug or device. Companies that came under scrutiny were Merck, SciClone, AstraZeneca, Bristol-Myers Squibb, Baxter and Eli Lilly (IPRM, September 2010). — Molly Cohen

**EMA Expects Slight Rise in Applications In 2011, Adopts Work Program**

The European Medicines Agency (EMA) expects a small rise from 2010’s 95 applications for marketing authorization to 97 this year.

At the EMA’s Management Board meeting on Dec. 16, the group used the expected rise in applications in adopting its 2011 work program and budget.

The board anticipates 40 applications for new human-use medicines, compared to last year’s 38; 12 new orphan medicine applications, down from 2010’s 14; and 42 generic applications, one more than last year’s 41.

Since the difference between this year’s expected applications and last year’s total is minimal, the 2011 staff cap at 567 agents should not be an issue.

The work program includes a 0.23 percent budget increase from last year to about $271 million for 2011. It also includes fee revenue of $209 million (compared to last year’s $198.8 million) as well as a $43.6 million contribution from the EU (which was about $51 million last year). However, the EU’s contribution to the special orphan medicines fund was reduced from about $10.7 million to $6.3 million this year.

The board also adopted the “Road Map to 2015,” which outlines three strategic areas for future action to support the EMA’s role as a regulator.

The road map was adopted after incorporating responses from 71 stakeholders ranging from EU institutions to patient organizations, healthcare professionals and health technology assessment bodies. — Molly Cohen

**EMA ‘Road Map to 2015’ Focuses on Public Health, Improved Access, Drug Safety**

The European Medicines Agency (EMA) identified three strategic areas for progress and change as part of its “Road Map to 2015” that will guide its activities and regulatory decisions.

The EMA’s road map, drafted last year and released this month, is a tool for the agency to take a long-term, proactive
approach to enhancing the pharmaceutical environment in the European Union. It identifies specific areas the agency will need to explore during the five years after it is published to maintain relevancy in the face of a changing regulatory atmosphere.

According to the document, “the focus for the next period will now be more directed towards the quality of the outcome of the Agency’s work and in particular how to increase such quality.”

As focal points for future agency action, the three areas will act as a guide to further the development and reinforcement of the EU Regulatory System Network, a pivotal cornerstone of the EU pharmaceutical landscape.

Addressing Public Health Needs

In the first area, addressing public health needs, the EMA plans to tackle the lack of medicines for unmet medical needs or neglected diseases. The agency plans to promote drug development by increasing the number of requests for scientific guidance related to these areas.

To reach this goal, the EMA will initiate investigations into the reasons for discontinuing research, focusing on orphan medicines. The agency is working on additional accelerated assessment schemes to encourage development of these treatments. The EMA also plans to launch initiatives to address the lack of antibiotics in development.

New and emerging science will also play a part in addressing public needs. The agency is working toward regulations for nanomaterials (see story, page 5). Similar technologies on the horizon include synthetic biology, as well as regenerative and personalized medicine. The EMA will pool scientific expertise to develop regulatory frameworks for these types of technologies as they progress.

Additionally, the EMA promises to take a more proactive approach to preventing and ending public health threats through enhanced preparedness for such outbreaks. The EMA recognizes three basic elements associated with each public health threat: the complexity of the problem, a global dimension and the need to find a quick solution. Therefore, the agency will work collaboratively with stakeholders and partners to review its preparedness mechanisms. It will also conduct “lessons learned” exercises after each major event to improve preparedness for the future.

The second strategic area focuses on facilitating access to medicines. The EMA will address the high attrition rate during the drug development process. The goal is to increase the number of successful marketing authorization applications and to better share scientific information on failed drugs. To reach these goals, the agency will encourage stakeholders’ involvement in the guideline preparation on medicine development. Additionally, the EMA will work to create incentives and a feasible system to share information from failed drug development.

The EMA will also reinforce the benefit/risk balance assessment model. The agency hopes this will lead to more inclusion of quantitative elements, improved elaboration of the rationale for official benefit/risk decisions and publication of the European Public Assessment Reports. A major component of the assessment model should take into account the availability of other treatment options for an unmet need. Additionally, the agency supports the setup of strategies to increase post-authorization information of medicine at the moment of licensing.

The EMA will also continue to improve the quality, regulatory maintenance and scientific consistence in regards to scientific review outcomes. The EMA expects this focus will lead to an increase in the consistency of outcomes during external surveys conducted by agency shareholders. The EMA sees two initiatives on this topic. The first will be to improve the agency as an information provider by increasing its transparency on the outcome of scientific reviews. Second, the agency will begin exploring, with health technology assessment bodies, the progress of a treatment from early development throughout a product’s lifecycle.

Optimizing the Safe Use of Medicines

The third area involves the safe use of medicines. The EMA plans to strengthen the evidence base in the post-authorization phase to create a model that would make post-authorization collection of data more widely available to the regulatory system.

The agency will also enhance patient safety by eliminating unnecessary risks to patients through a revised risk management concept targeting novel pharmacovigilance methodologies. The hope is that such efforts will make it a reference point on information for medicines, which would put high quality information on medicines at the disposal of the EU regulatory system network.

The EMA also expects an improved decision-making process to utilize conclusions from research projects to provide input into future decisions.

The road map will be formally adopted later this year following public consultations. — Molly Cohen

To view the text of the road map, click here.

UK Moves Toward Appraising Avastin as a Cheaper Macular Degeneration Treatment

The UK’s National Health Service (NHS) is waiting for the go-ahead to begin an appraisal for using Roche’s Avastin as a treatment for wet age-related macular degeneration (AMD), even though the biologic is not licensed for that indication.

The NHS’ National Institute for Health and Clinical Excellence (NICE) is looking into an appraisal for Avastin (bevacizumab), which is frequently used off-label as a
cheaper alternative to Lucentis (ranibizumab), to treat wet AMD, by splitting bevacizumab into smaller pieces.

In an unusual move, the country’s Department of Health (DoH) requested that NICE explore the value of advising the NHS on the use of Avastin for AMD.

Roche, the manufacturer of both treatments, offers Lucentis as a smaller, modified form of Avastin that is licensed to treat wet AMD. Avastin is indicated for the treatment of various types of cancer, but shows similar benefits in treating AMD as Lucentis.

When asked by IPRM why Roche is not interested in a license for Avastin as an AMD treatment, company spokeswoman Charlotte Arnold said the company is pursuing cancer treatments with Avastin since Lucentis is already licensed for wet AMD.

AMD occurs when there is new blood vessel growth in an area of the eye where it is not supposed to occur. Avastin and Lucentis stop that growth by targeting and inhibiting the function of a natural protein called vascular endothelial growth factor.

**Significant Price Difference**

While both drugs require multiple treatments, there is a significant difference in their price. According to the Center for Preventive Ophthalmology and Biostatics (CPOB), one treatment of Lucentis costs about $2,000 while an Avastin treatment for AMD costs around $50 to $100.

In December, NICE released a report on comments made during a July workshop during which medical professionals discussed the viability of an appraisal for Avastin. The main conclusion is that there was support for an appraisal of intravitreal Avastin for eye conditions. However, the report noted “appraisal would need to be conditional on, or incorporate the assessment of, the safety and quality of intravitreal bevacizumab by a regulatory body.”

NICE is awaiting a DoH decision on whether or not to refer the drug for an official appraisal.

Meanwhile, Novartis, which markets Lucentis in the UK, is not actively seeking a way to lower the drug’s price to put it on par with Avastin. “Currently, ranibizumab is offered through the Ranibizumab Reimbursement Scheme … designed to ensure ranibizumab is available on the NHS to all eligible patients with wet age-related macular degeneration,” Novartis spokeswoman Sophia Hosseini told IPRM. “The RRS will continue until March 31, 2012, or when the next NICE guidance is issued.”

Hosseini also pointed out that, as reflected in the NICE report, Novartis has offered to work with the DoH to find ways to make Lucentis more accessible.

While there is support for Avastin as an AMD treatment, some workshop participants had concerns regarding the unproven safety of Avastin in the indication.

Hosseini agrees, saying, “any short-term cost savings made by using bevacizumab must be weighed against the increased risks associated with use outside of its licensed indications, without review or collection of sufficient long-term efficacy and safety data.”

Medical groups have voiced apprehension on Avastin’s safety and have been hesitant to show support for the biologic until it has been reviewed for safety in treating AMD.

The Royal National Institute for the Blind (RNIB), which allegedly receives funding from Novartis, said it “has concerns over the use of Avastin for the treatment of wet AMD because no trials have been performed to establish its safety and efficacy or use in the eye.”

The RNIB also suggests that for physicians who recommend Avastin, “it is essential that they provide patients with full information about all available options.”

**Compounding Concerns**

Meanwhile, the Royal College of Ophthalmologists pointed out, “Genentech, and partner Roche … recently raised concerns about the compounding of Avastin into smaller doses for intraocular use as it is not designed, manufactured or approved for such use.”

As the manufacturers of the product, the companies added they are concerned “that compounding may contaminate the product.”

While Avastin’s safety has not been reviewed in AMD, the college says, “it is hoped that using relevant expertise through a regulatory body will allow future appraisal by NICE of bevacizumab for treating eye conditions.”

As a result of the debate, two head-to-head trials comparing Avastin and Lucentis are underway. The IVAN trial will compare the efficacy and safety of the two biologics. It will also determine whether the number of treatments can be reduced.

The study, funded by the UK government, will randomize patients to various treatment combinations and will test eyesight at each visit. Participants will be compared after one- and two-year follow-up sessions.

In the U.S., CPOB is funding the CATT trial, a multi-centered, randomized, clinical trial with the same endpoints. The trial will enroll 1,200 participants at 44 sites over 24 monthly visits. Participants will be randomized into four treatment groups: Lucentis every four weeks for one year, Avastin every four weeks for one year, Lucentis on variable dosing for two years or Avastin on variable dosing for two years. The results of the two trials are expected in, respectively, late 2011 and early 2012. — Molly Cohen
Nanomaterials Still Undefined by EU Experts, Delaying Regulations

Before devicemakers can expect guidance on nanotechnology, EU regulators must first decide what a nanomaterial is.

In grappling with the issue, the European Commission’s (EC) Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) acknowledges the complexity and uncertainties involved in trying to come up with a one-size-fits-all definition.

While size is critical to the definition, determining what that size should be and measuring it are challenges that must be addressed, SCENIHR says in an opinion released last month.

The committee recognizes safety evaluations and risk assessments of nanomaterials depend on a decisive definition. “With the expected increase in the applications of nanotechnology, there is an urgent need to identify what can be considered as a nanomaterial by clear unequivocal descriptions,” it says.

While SCENIHR did not propose a definition, it offers a few conclusions:

- Since physical and chemical properties of materials can change with size, there is no scientific justification for a single upper and lower size limit that can be applied to all nanomaterials;
- No single methodology is applicable to all nanomaterials; and
- Size is universally applicable to define nanomaterials and is the most suitable measure.

“Not only is size itself important, but also the method used to measure it,” the committee says. In addition to developing a definition for nanomaterials, regulators need to develop and validate standardized methods to determine the size of the materials, along with the corresponding distribution, to ensure comparability of test results, it adds.

The committee recommends a defined size range to facilitate uniform interpretation of a nanomaterial. It suggests 1 nm for the lower limit, with some exceptions to allow for specific entities such as graphene, clusters and complex hybrid molecular structures. It also recognizes that the distinction, at this level, of molecules, nanoclusters and nanoparticles becomes unclear.

Setting the upper end of the size range is more difficult, SCENIHR says, as no scientific evidence favors a single upper limit. While an upper limit of 100 nm is commonly used, there is no justification for it, and it may be too limiting.

Instead, the committee suggests a three-tiered approach using intermediate thresholds: materials greater than 500 nm, those ranging from 100 nm to 500 nm and those from 1 nm to 100 nm.

In adopting a definition, SCENIHR advises the EC to consider an over-arching one that would include next-generation nanomaterials and would not become obsolete too quickly.

The committee also discusses other challenges in regulating nanomaterials. Current risk assessment methods, for instance, may be applicable for nanomaterials in general, but they may not be sufficient to address all the hazards involved. Thus, current assays may “need to be supplemented by additional tests, or replaced by modified tests, as it cannot be assumed that current scientific knowledge” has identified all potential adverse effects of nanoparticles, it says.

Agencies in the EU and the U.S. have been struggling with how to regulate nanotechnology for several years. A 2008 UK environmental report called for urgent testing and regulation to control the rapidly developing field, and FDA scientists are trying to expand their knowledge (IPRM, December 2008).

Noting a lack of nanotech-specific regulations, the EC adopted a Code of Conduct for Responsible Nanosciences and Nanotechnologies Research in 2008 aimed at minimizing the risk of environmental, health and safety consequences from the manufacture and use of nanotechnology.

SCENIHR’s opinion on defining nanomaterials is available at ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_032.pdf. — Molly Cohen

European SMEs Get Online Registry To Foster Nationwide Partnerships

The European Medicines Agency (EMA) has launched a public registry of small and medium-sized enterprises (SMEs) in the pharmaceutical and medical device industries throughout Europe to facilitate partnerships between companies.

The EMA will enhance its existing list of SMEs, which currently only includes each business’ country of origin, through two phases.

In the first phase, the registry will provide contact details for each company as well as its business focus areas and head count. In the second phase, which begins at the end of March, company pipeline and product profiles will be added to each company’s listing.

“The aim of the registry is to facilitate cooperation, networking and synergies between SMEs by providing them with details about other SMEs who are working in the field of … human medicines,” EMA spokeswoman Monika Bensetter told IPRM.

The registry will be updated quarterly and only SMEs that have been officially recognized with SME status can be included in it. It is designed to meet demands for more information and greater interaction between Europe’s SMEs as they are an important source for economic growth, innovation and employment.
While the registry is open to the public, only SMEs who are registered with the EMA will be listed.

In 2010, the number of companies assigned SME status increased by 10 percent compared to the previous year. As of mid-December, 507 companies were registered as SMEs and another 58 companies were under review for the designation.

Launching the registry is the most recent step in the EMA’s ongoing transparency initiative.

The agency has been providing regulatory assistance, assistance with translations, fee reductions, exemptions, deferrals and the certification for advanced therapy medicinal products since 2005.

The SME registry is available at fmapps.emea.europa.eu/SME/.


**EU, India Drop WTO Generics Dispute**

**To Focus on FTA Talks**

As part of fair trade agreement (FTA) negotiations, the EU and India have unofficially resolved their 2009 World Trade Organization (WTO) dispute over repeated seizures of generic drugs en route from India to other countries.

The WTO dispute was initiated by India after the EU repeatedly seized generic drugs originating in India as they passed through European ports on their way to Brazil. They were seized on the grounds of patent infringement.

India disagreed with the patent infringement claims. Brazil agreed with India and initiated an additional WTO dispute with the EU on the same topic.

As a result of India and Brazil’s concerns, the EU is examining its existing rules that triggered the WTO disputes to increase clarification and prevent any misunderstanding.

While consultations with Brazil over the dispute are ongoing, the EU and India have agreed to suspend their dispute to focus on enhancing trade. The dispute is not officially resolved, but the EU and India believe it is best to cease discussion on the topic, according to the EU.

Taking the dispute into account, the EU plans to make sure the patent rights chapter of any future FTA reflects the views of both parties. A new agreement is expected to be finalized in the spring.

The document is expected to improve market access for goods and services, including all trade except for public procurement. Bilateral trade is expected to exceed $210 billion by 2015.

The EU-India WTO dispute is available at www.wto.org/english/tratop_e/dispu_e/cases_e/ds408_e.htm.

The EU- Brazil WTO dispute is available at www.wto.org/english/tratop_e/dispu_e/cases_e/ds409_e.htm. — Molly Cohen

**Europe to Increase Collaboration With Asian Health Agencies**

The European Directorate of the Quality of Medicines & Healthcare (EDQM) plans to foster global discussion and collaboration in drug safety and other areas through agreements with several Asian health agencies signed last month.

The EDQM signed memorandums of understanding with Korea’s National Institute of Food and Drug Safety, the Korea Food and Drug Administration and the Chinese National Institute of Food and Drug Control to strengthen collaboration between the groups.

The EDQM’s goal in signing these agreements is to increase awareness of the importance of quality and safe medicines, establish a basis for and promote cooperation between each agency, and identify areas of shared concern for possible future partnership.

Areas identified by the EDQM might include developing monographs, establishing and managing reference substances, (See MoU, Page 7)

An Interactive Workshop Presented by LearningPlus and FDAnews

**From Training to Learning**

**Improving GMP Performance**

**An FDAnews Conference**

**March 28–29, 2011 ¢ Bethesda, MD**

**Doubletree Hotel Bethesda**

While there are more than 20 references to training within the FDA’s GMP regulations, the vagueness of the requirements is a constant source of confusion for companies, their training officers and their employees. Unfortunately, GMP trainers are often expected to create a training course, get everyone’s signature on the “happy sheet,” and go away. As a result, these reportedly trained professionals can’t possibly have learned the material.

This critical workshop thoroughly covers the best way to convey your GMP knowledge to your staff efficiently, accurately and effectively. Through a series of hands-on exercises, you’ll develop and deliver a clear and concise GMP training program that will fully prepare your employees to handle GMP with confidence.

Register online at: www.fdanews.com/2992A

Or call toll free: (888) 838-5578 (inside the U.S.) or +1 (703) 538-7600
MoU, from Page 6

conducting research projects, organizing scientific training conference and workshops, and exchanging staff.

“Signature of these Memoranda of Understanding ... recognizes the importance of developing a long-term strategy at international level to ensure the quality and safety of medicines made available to the public,” said EDQM director Susanne Keitel. — Molly Cohen

UK Releases Consultation on Value-Based Drug Pricing

A proposed value-based approach to the pricing of branded medicines, which would allow the UK government the power to set prices, has drawn criticism from industry who fear the move will hamper R&D and access to new therapies.

The system, put forward by the Department of Health (DoH), aims to give patients better access to effective and innovative medicines while encouraging pharmaceutical companies to develop innovative medicines. The current system allows companies to set their own pricing for drugs.

“A key objective of value-based pricing is to change the incentives within the medicines pricing system, to encourage the development of new medicines in areas of greatest unmet need and to promote genuine innovation,” the DoH says.

The system was outlined in a document for consultation, released Dec. 16, that sets out principles forming the base of the system and how it would work across the country. The DoH will accept industry comment through March 17.

Although the DoH says that many stakeholders have shown support for the new system, industry seems to be wary of the potential for unexpected pitfalls.

“The priority in any new system must be rapid and consistent patient access to new medicines—value is meaningless without consistent access,” says Richard Barker, director general of the Association of the British Pharmaceutical Industry. “Any new system must also fairly recognize and reward innovation and investment in research and development,” he adds.

That sentiment was echoed by Adrien Towse, director of the Office of Health Economics (OHE), an independent research, advisory and consultancy service that focuses on health care. In a September 2010 article published in the British Journal of Clinical Pharmacology, Towse warns of the loopholes the new scheme might allow.

“Instead of adding to uncertainty the institutional arrangements for assessing value should seek to be predictable and science-based, building on NICE’s [the National Institute for Health and Clinical Excellence] current arrangements,” Towse adds.

Likewise “increasing the uncertainty in the UK NHS [National Health Service] market through government price setting will reduce incentives for [research and development] and for early UK launch.”

The release of the draft follows the proposal for a value-based drug pricing scheme, originally instituted by the UK’s Conservative-Liberal Democrat Coalition (IPRM, June 2010).

“Under the existing policy, new drugs are assessed for their cost effectiveness based on a price which the company has the freedom to set,” the DoH says. “The aim of a value-based pricing policy will be to increase patient access to beneficial drugs by ensuring that important new medicines are obtained at a price that reflects their value.”

Policy Would Increase Patient Access to Drugs

A value-based system should allow the NHS to more effectively provide patients across the board access to treatments that could be beneficial and improve their health.

The new system, which would go into effect at the end of 2013, would apply to new drugs on the market starting on Jan. 1, 2014. Branded medicines released on the market before that date would be subject to a successor scheme to be developed alongside the value-based system.

Under the new system:

- The government would set a range of thresholds or maximum prices reflecting the different values that medicines offer, with higher thresholds for medicines filling an unmet need or wider societal benefits;
- The value of products would be assessed and compared to benefits that could be gained if the funds were used to help other patients, possibly based on a Quality Adjust Life Years (QALYs) system; and
- NICE would be an independent government entity that establishes standards for care pathways (IPRM, August 2010).

NICE’s role would evolve in two stages, according to OHE. In the first phase, NICE would set prices that would make a drug the most cost effective in different patient subgroups and the DoH would negotiate the price with the company.

In the second phase, “NICE would be merged with its Scottish and Welsh equivalents and be given DoH’s power to set prices for medicines when used by the NHS.”

The new pricing system would contrast drastically with the current pricing system, the Pharmaceutical Price Regulation
Scheme (PPRS), which is an agreement between the pharma industry and the government that seeks to create a balance between prices paid by the NHS and a fair return for industry.

However, the DoH believes “freedom of pricing for new drugs puts the NHS in the position of either having to pay high prices that are not always justified by the benefits of a new drug, or having to restrict access.”

To transition from the PPRS to the value-based approach, the government created a £50 million ($77 million) interim cancer drug fund program available from October 1, 2010 until it establishes a Cancer Drugs Fund beginning April 1 in an effort to increase access to oncologics.

Meanwhile, NICE’s role during the interim period will continue to ensure patient access to clinically and cost effective drugs and treatments, according to the DoH. It will continue to appraise new drugs until the value-based pricing system is implemented in 2014.

Understanding that there will be issues with the initial phases of the pricing scheme, the DoH says “once the policy is ready for implementation, it is intended that the effects of the policy would be monitored and a review process put in place, although it is currently too early in the policy development cycle to consider how this may operate with any relevant level of detail.”


NICE to Create New Quality Standards for 31 Clinical Areas

As part of the UK National Health Services’ (NHS) outcomes framework for 2011/12, the National Institute for Health and Clinical Excellence (NICE) will produce quality standards for 31 clinical areas.

NICE’s quality standards aim to help healthcare practitioners deliver services through specific statements that dictate high-quality and cost-effective patient care in treatment areas. It also potentially impacts drugmakers as statements include elements or indicators to help NHS assess the quality of therapies and improvements needed.

The standards play into the framework, which was published last month, by setting a national overview of aims and objectives for the NHS in improving patient outcomes. The framework also creates indicators used to hold the NHS Commissioning Board accountable for outcomes delivered through health services.

The quality standards are developed from NICE guidance or other NHS evidence and are aimed at patients and the public, clinicians, public health practitioners, commissioners and service providers.

Topics for quality standards are referred to NICE by ministers from suggestions of the National Quality Board. The 31 topics slated for quality standards include chest pain, antenatal care, asthma, bipolar disorder, colorectal cancer, diabetes, hepatitis B, drug use disorders, epilepsy, head injuries, hip fractures, lung cancer, myocardial infarction, ulcerative colitis, meningitis, migraines, nutrition, osteoarthritis, ovarian cancer, postnatal care, ulcers, prostate cancer, pulmonary embolism, reflux disease, safe prescribing and schizophrenia.

These topics will join four clinical areas that already have quality standards developed by NICE and include stroke, dementia, neonatal care and venous thromboembolism (IPRM, August 2009). In addition, nine other topics are currently in development.

NICE aims to produce 150 quality standards over the next five years.

NICE’s list of topics slated for new clinical areas is available at www.nice.org.uk/newsroom/news/ThirtyOneNewQualityStandardsToBeDeveloped.jsp.


— Molly Cohen

Drug Safety Reporting in the EU
From Clinical Trials to Postmarket Pharmacovigilance

An FDA News Publication

If you’re going to conduct clinical trials or sell drugs in the EU, the way you handle safety reporting will be essential to your success.

But navigating EU pharmacovigilance requirements is a complex task that starts in the early stages of drug development and extends right through the drug’s life, and it varies subtly from one member state to the next.

Don’t base your access to EU markets on what you think is required to comply with drug safety reporting requirements. Count on this new Management Report to help you know for certain.

Order online at:
www.fdanews.com/33120A
Or call toll free: (888) 838-5578 (inside the U.S.)
or +1 (703) 538-7600

Price: $377
Counterfeit Medical Products Under Scrutiny of Medicrime Convention

Drug manufacturers will be held accountable for the legitimacy of their products under the first binding international document to deal with counterfeit medical products.

The Council of Europe’s Medicrime Convention introduces preventive and penal measures for the criminal counterfeiting of medical products on national and international levels.

The convention, which includes 47 countries to date, criminalizes:

- Manufacturing of counterfeit drugs;
- Supplying, offering to supply and trafficking in counterfeit drugs;
- Falsifying documents; and
- Marketing of drugs that do not comply with conformity requirements.

Adopted last month, the convention includes guidelines for national and international cooperation. A monitoring body will be created, with representatives from each member country to implement the convention.

“The Council of Europe has long been concerned about the absence of harmonized international legislation, non-deterrent sanctions disproportionate to the harm caused to patients, and the involvement of criminal organizations which operate across borders,” Swissmedic, the Swiss agency for therapeutic products, says.

Counterfeiting is a multi-billion euro industry that is often linked to organized crime and drug trafficking, according to the Council of Europe.

Counterfeit medical products are more of a threat in developing countries. For instance, counterfeits make up less than 1 percent of the market value in developed countries but more than 50 percent in developing countries, according to the World Health Organization (WHO).

Much of the marketing of counterfeit drugs is done online. The creation of the Medicrime Convention follows an international offensive against online distributors of counterfeit medicinal products that resulted in the October seizure of more than 1 million pills at an estimated $2.6 million value (IPRM, November 2010).

Other countries and organizations are taking similar efforts to go after counterfeiters. The Anti-Counterfeiting Trade Agreement, for example, is being negotiated by Australia, Canada, the EU, Japan, Korea, Mexico, Morocco, New Zealand, Singapore, Switzerland and the U.S.

Similarly, the WHO has introduced initiatives to combat counterfeit products globally (IPRM, February 2009).

The draft convention and related materials are available at www.coe.int/t/DGHL/StandardSetting/MediCrime/Default_en.asp. — Molly Cohen

MoU Means Increased Cooperation Between Ireland’s Healthcare Regulators

To maximize efficiency and effectiveness and to solidify a pathway to continue working together, the Pharmaceutical Society of Ireland (PSI) and the Health Information and Quality Authority (HIQA) have signed a memorandum of understanding (MoU).

PSI is the country’s pharmacy regulator and HIQA sets standards for delivering healthcare services.

The MoU, signed last month, aims to increase the mutual cooperation of the two organizations. “This memorandum of understanding provides HIQA and the PSI with an excellent opportunity to demonstrate our commitment to driving high quality and safe care for people using our health and social care services,” said Tracey Cooper, HIQA chief executive.

The groups plan to work together to make the most of their regulatory functions for older people in residential centers, nursing homes or other designated centers for people of advanced age.

The MoU also includes guidance on information exchange.

“There already exists a strong cooperation between the PSI and HIQA, so we are pleased to formalize this arrangement towards ensuring more effective regulation in common areas of activity. This memorandum of understanding is designed to structure this relationship and meet each organization’s aims and objectives,” said Ambrose McLoughlin, PSI’s registrar and chief executive. — Molly Cohen

Poland’s Draft Reimbursement Act Will Impact Pharma Industry

Draft legislation in Poland offers the potential for improvements in the reimbursement of innovative products, but it also could increase financial risks for companies and negatively impact sales, according to analysts.

Poland’s “Act on the Reimbursement of Pharmaceuticals, Foodstuffs Intended for Particular Nutritional Purposes and Medical Devices” aims to control reimbursement as well as price markups for wholesalers and retailers.

After going through development for over a year, a draft of the legislation has been passed to Parliament for its first reading. It is expected to come into full force in 2012 after the government goes through negotiations with industry. In the meantime, healthcare experts are looking for potential positive and negative impacts the act might have on Poland’s pharmaceutical industry.
“The proposed amendments are revolutionary and could lead to a radical and fundamental change in existing business models and in the rules on marketing activities, and could even affect sales structures,” say analysts at Domanski Zakrzewski Palinka, a Polish life sciences law firm.

The act introduces a reduced official wholesale margin of 5 percent, and retail margins for reimbursed drugs and fixed official sales prices to be set through negotiations between the Ministry of Health and drug manufacturers. As a result, there may be a restriction or elimination of discounting, which could affect competition and companies’ profitability.

The act would allow applicants to challenge negative decisions before administrative courts. However, a weak point of the system, according to Łukasz Bobel, a partner with Polish law firm Weremczuk Bobel i Wspolnicy, is a mechanism for setting reimbursement limits and limit groups. “They are to be set, not in individual decisions on reimbursement, but in announcements published by the Ministry of Health that are not formally a source of law and cannot be legally challenged,” he says.

Reimbursement Cap

Despite the reduced margins for Polish wholesalers and pharmacies, the fixed markups might have positive implications for drugmakers thanks to tighter controls on drug prices at the consumer level. These controls should ensure stability between drug producer and pharmacy prices, says Business Monitor International (BMI), an independent provider of data and analysis for industries around the world.

However, BMI adds that the legislation also includes risks for drugmakers through the introduction of further pharmacoeconomic analysis, a limit on drug spending by the Polish National Health Fund (NFZ) and a rebate to be paid by manufacturers to the Ministry of Health.

IHS Global healthcare analyst Brendan Melck told IPRM he expects discussions between the Ministry of Health and drugmakers to establish new drug prices based on the proposed regulations.

One of the most controversial provisions is a 17 percent reimbursement cap of total NFZ spending. If the threshold is exceeded, drugmakers of reimbursed medicines would have to pay the NFZ an amount proportionate to the share of their products in excess of reimbursement spending. This provision is of particular concern to drug manufacturers since “it imposes a serious financial risk that cannot be managed by pharmaceutical companies,” Bobel says.

Domanski Zakrzewski Palinka analysts say this particular provision has four major effects on business: potential major restrictions on marketing activity, taking on a serious financial risk that cannot be fully controlled by a firm’s position, potential need to take out insurance, and the need to restructure agreements with parent companies and foreign suppliers.

Melck said the new reimbursement cap might not necessarily hamper drug companies: “When you consider that in 2009, 18.9 percent [of NFZ spending] went to reimbursement of medicines, [the new cap] would mean a reduction, unless there’s a major increase in health expenditure overall. If you take the positive attitude that there will be an increase in the next three years, then it’s not such a bad thing. But if it goes at the same rate it has recently, then it might be problematic for drug companies.”

Melck also highlighted a concern voiced by other consultants in that Poland’s three pathways to reimbursement — pharmacy, chemotherapy and therapeutic programs — will all “be fighting over that cake more because they’ll see it as a restricted thing.”

But drugmakers’ biggest concern, he added, is the threat of payment to cover NFZ overspend. “They could be liable to pay out quite a lot.”

Additional Costs for Drugmakers

Additionally, a new tax presented in the draft act would require drugmakers whose products get approved for reimbursement to pay 3 percent of the official fixed sales price multiplied by the number of unit packages sold in a given year. The tax will create additional costs to drug developers through reduced profits from reimbursed products, according to Domanski Zakrzewski Palinka.

However, Melck says this tax “is not particularly unusual [since] in Italy and Hungary, the industry faces similar charges.”

One positive item in the legislation for companies is a potential provision that offers risk sharing between the NFZ and drugmakers. This element would make the pay-back mechanism not applicable if the company was asked to pay reimbursement overages as a result of the reimbursement cap, according to Bobel.

Although the risk-sharing provision is reportedly still vague, Melck noted, “I think that it will be a positive thing and will go hand-in-hand with having a great number of innovative drugs and will mean more feasibility for those drugs to be accessed.”

Poland’s pharmaceutical industry must wait for the final provisions to be released before the implications of the act are clear. “I think what they want to do is increase access to new, innovative drugs and make it easier for people to get treatments compared to in the past when it was hard to get those,” says Melck.

However, approval of the act is slow. “They’re trying to do a lot quite quickly … all has to be done in a proper way,” says Melck. “It might take a long time because they potentially intend to go through and establish new prices for all the drugs reimbursed in Poland based on the reimbursement act. That’s a huge job.”

But, Melck added, “it’s probably a good thing there’s a government openness to negotiations with the industry.
Maybe it will be a positive change that during [2011], different sides … will have a chance to have more to say.”


Industry Says Combination Technologies Will Need More Tools for Regulation

Citing a range of new technologies that cross the line between devices and drugs, the Medical Technology Association of Australia (MTAA) is urging regulators to develop more tools to assess combination products.

Australia’s current system poses many challenges for codependent technologies, but the biggest issues are fragmentation, lack of coordination and replication, MTAA says in response to a proposed methodology to assess combination products.

The methodology, proposed by Australia’s Department of Health and Ageing, focuses on a simple pairing of a diagnostic test with a drug. MTAA notes that the draft does not cover the many hybrid and codependent healthcare technologies available.

The department recognized that shortcoming when it released the draft, calling it “the first step in formulating a framework to manage the evidence and process issues involved in dealing with codependent technologies.”

It plans to use comments on the draft, which were due last month, to develop more comprehensive guidelines that can address more complex combination products.

MTAA offers numerous examples of codependent technologies that have faced regulatory challenges, including continuous glucose monitors connected to insulin pumps. The pump is reimbursed, but the monitor isn’t, which means the patient may have to pay for it. “As insulin pumps become technically more responsive to continuous glucose monitors, the clinical benefits of the working partnership of the two devices will have more to offer patients, and its lack of reimbursement will have greater impact,” the trade association says.

MTAA’s comments are available at www.mtaa.org.au/pages/images/MTAA submission to DoHA on co-dependent technologies Dec 2010.pdf. — Molly Cohen

TGA Releases Guidance for Non-eCTD Electronic Submissions

Australia’s Therapeutics Goods Administration (TGA) is providing direction for companies who choose to make electronic drug applications utilizing a non-electronic common technical document (eCTD) format.

According to the Jan. 4 draft guidance, the TGA will accept applications in either non-eCTD electronic submission (NeeS) or eCTD format. The agency is also publishing a separate guidance on requirements for eCTD dossiers.

The major difference, according to the guidance, between the eCTD and NeeS format is that two XML files and the util folder are not present in a NeeS submission. Therefore, “navigation through an electronic submission is greatly enhanced by the intelligent use of bookmarks and hypertext links,” the draft says.

The draft guidance delineates all of the requirements for a NeeS application including appropriate document naming patterns, table of contents, formatting, security and acceptable media standards (CD-ROM, CD-R and DVD-R).

One NeeS application can cover all dosage forms and strengths for a product, unless the sponsor wishes to submit separate applications for different strengths of a product.

The application form should also be included as a PDF file and a signed paper copy should also be provided.

The release of the guidance follows an earlier guidance that requires submission dossiers for Category 1 and 2 prescription medicines to include a hard and electronic copy (IPRM, November 2010).

A copy of the draft guidance is available at tga.gov.au/pmeds/pmbpi-submissionnees.pdf. — Molly Cohen