IN brief

Polar biotech

Dozens of companies are mining the Arctic's biological resources for their biotech potential, a United Nations report has found. *Bioprospecting in the Arctic* identified 31 patents and patent applications for inventions based on Arctic genetic resources. The patents cover several areas including enzymes, anti-freeze proteins and bioremediation, and are derived from marine and hot-spring microbes, cold-water fish, mammals and plant extracts. The industry is well established, says David Leary, author of the report and post-doctoral fellow at the United Nations University Institute of Advanced Studies in Tokyo. Leary identified 43 companies involved in researching or commercializing Arctic-derived biotech. He was surprised at the scale of the activity. "Some policy makers are under the impression that it is not happening there," he said. Organisms in the Polar Regions have adapted to the harsh conditions, including extreme temperature and salinity, so offer the potential to develop novel biotech applications. "Organisms living in cold waters have enzymes with high activity," says Gerd Nilsen, a product manager at Biotec Pharmacon, a biopharmaceutical company based in Tromsø, Norway, that has commercialized a recombinant cod liver enzyme—uracil-DNA-glycosylase—for use in molecular diagnostic kits. The threat of commercial exploitation in the poles is real, Leary cautions. "Where there is an environmental impact…you have to think about regulating it," he says. *–Hannah Hoag*

Deaths stalk GLP-1 agonist

The type 2 diabetes drug Byetta (exenatide) has been linked to the deaths of six people with acute necrotizing or hemorrhagic pancreatitis, prompting the US Food and Drug Administration to call for stronger label warnings. Amylin, of San Diego, and Eli Lilly, of Indianapolis, which co-market the drug, admit the association between Byetta usage and acute pancreatitis is possible, although it is unclear what role glucagon-like peptide 1 (GLP-1) agonists played in causing the fatal symptoms. Individuals with diabetes are normally three times more likely to develop the condition than nondiabetics, partly because conventional treatments for type-2 diabetes are also associated with pancreatitis. Daniel Drucker, director of Banting and Best Diabetes Centre at the University of Toronto says more pancreatitis data across different classes of antidiabetic drugs are needed to "determine whether the disease is more or less commonly seen with Byetta versus other antidiabetic agents." Byetta is a synthetic peptide with 53% homology to human GLP-1. It is the first in a new class of drugs called GLP-1 agonists, which mimic the hormone's ability to induce insulin secretion and downregulate blood glucose levels after eating. Drucker, who consults for GLP-1 agonist producers, including Amylin, acknowledges that clinicians are "somewhat apprehensive about GLP-1 therapies," but expects opinions to change once clinical data emerge over the next year. Byetta's main competitor is Liraglutide, a long-acting human GLP-1 agonist produced by Novo Nordisk, of Copenhagen, which could be approved by mid-2009. *–Jodi Hyer*

Table 1 FDA posts its first quarterly list of drugs in review for potential safety issues

Generic name (Brand name) or product class	Potential signal of serious risk/new safety information
Arginine hydrochloride injection (R-Gene 10)	Pediatric overdose due to labeling/packaging confusion
Desflurane (Suprane)	Cardiac arrest
Duloxetine (Cymbalta)	Urinary retention
Etravirine (Intelence)	Hemarthrosis
Fluorouracil cream (Carac) and ketoconazole cream (Kuric)	Adverse events due to name confusion
Heparin	Anaphylactic-type reactions
Icodextrin (Extraneal)	Hypoglycemia
Insulin U-500 (Humulin R)	Dosing confusion
Ivermectin (Stromectol) and warfarin	Drug interaction
Lapatinib (Tykerb)	Hepatotoxicity
Lenalidomide (Revlimid)	Stevens Johnson Syndrome
Natalizumab (Tysabri)	Skin melanomas
Nitroglycerin (Nitrostat)	Overdose due to labeling confusion
Octreotide acetate depot (Sandostatin LAR)	Ileus
Oxycodone hydrochloride controlled-release (Oxycontin)	Drug misuse, abuse and overdose
Perflutren lipid microsphere (Definity)	Cardiopulmonary reactions
Phenytoin injection (Dilantin)	Purple Glove Syndrome
Quetiapine (Seroquel)	Overdose due to sample pack labeling confusion
Telbivudine (Tyzeka)	Peripheral neuropathy
Tumor necrosis factor (TNF)-alpha blockers	Cancers in children and young adults

nothing to fix this. One example he cites is the decision of the agency in October 2007 to ask makers of all phosphodiesterase type 5 inhibitors for erectile dysfunction and pulmonary arterial hypertension to put label warnings on their products about possible hearing loss, even though the FDA admitted no causal relationship had been shown.

The same happened with Chantix (varenicline), the smoking cessation drug from Pfizer that the FDA said might lead to suicide and thoughts of depression. In another example, Basel-based Roche and GlaxoSmithKline of London agreed in March 2008 at the FDA's urging to revise labels of the influenza drugs Tamiflu (oseltamivir) and Relenza (zanamivir), cautioning prescribers about unproven but potentially fatal neuropsychiatric events. In early September, under the FDAAA's adverse-event reporting system, the FDA published a list of 20 drugs pegged as having "potential safety issues" (**Table 1**). The FDA assembled the list based on its review of adverse event reports, though a drug's appearance on the list does not mean that the drug is unsafe, the agency said, only that closer examination is warranted and they are looking into it.

A year after it passed into law, perceptions over the FDAAA's main impact have shifted somewhat. At the outset, phase 4 clinical trials and REMS were viewed as the key elements of the new legislation. Bradshaw argues, however, that the FDA's new labeling authority could have the largest impact. "I have great confidence in the current chief counsel," he says. "The problem is that 99% of these labeling requests the chief counsel will never hear about," since word will go up the ladder "only in the rare cases where the company objects." One probable outcome is that more companies will object, says attorney Price. Bradshaw agrees, though he is overall optimistic about FDAAA because it gives the FDA "breathing room to approve much-needed drugs, and gives folks the comfort of knowing" that REMS and phase 4 trials (along with label changes) can protect patients. Shearer agrees, adding that the somewhat more involved and time-consuming drug application process entailed by FDAAA should help. "Do the job right up front, and you don't have to pay the piper later," he says.

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New product approval

Cinryze (C1-esterase inhibitor)/Lev Pharmaceuticals (New York). (The firm is merging with ViroPharma, of Exton, Pennsylvania.)

The US Food and Drug Administration approved the drug Cinryze, a drug prepared from human plasma, for routine prophylaxis against angioedema attacks in adolescent and adult patients with hereditary angioedema. Cinryze, a C1-esterase inhibitor or C1-INH, has been used in Europe for 30 years but has never before been introduced in the US. There is a post-approval requirement for Lev to conduct a clinical study on safety, which will monitor thrombotic adverse events, efficacy and immunogenicity of higher-than-labeled doses of Cinryze for routine prophylaxis.