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an exclusive weekly report on Food and Drug Administration policy, regulation and enforcement

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FDA FLOATS DRAFT LEGISLATION TO NIP DRUG MAIL ORDER IMPORTATION

FDA is floating draft legislation that would reduce the administrative hoops the government must jump through before it can send back or destroy illegal prescription drugs coming into to the country by international mail, according to an FDA source. Specifically, the legislation would allow FDA to bypass the 15-day notice period the agency must currently give the person receiving the drug.

The source said FDA discussed its legislative proposal with House Energy and Commerce Committee staff in a meeting last week. The plan would eliminate the 15-day notice that FDA is currently required to give the

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CONGRESS GIVES DEVICE INDUSTRY DRAFT USER FEE COMPROMISE TO REVIEW

House Energy and Commerce Committee staffers have given medical device industry trade groups a draft of a compromise device user fee plan that would establish a two-tier system for premarket approval applications (PMAs) while keeping a single rate for 510(k) applications for "generic" devices that are similar to devices already on the market, according to a source at the Medical Device Manufacturers Association (MDMA). The staff asked industry trade groups to vote on the plan by the end of Thursday (Aug. 8).

The source says MDMA's members approved the plan "with a few limitations on the two-tier system." The

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BIO MAY DROP CAPS IN INDEMNIFICATION PLAN IN BID TO GAIN SENATE PASSAGE

With Congress again interested in finding a way to shield companies that produce couterterrorism products from lawsuits, the biotechnology industry may begin shopping compromise language in a bid to appease the trial lawyers and gain Senate passage. The Biotechnology Industry Organization (BIO) is considering dropping its earlier insistence that legislation include caps on the amount of money that plaintiffs may seek in a lawsuit for noneconomic damages, according to an industry source.

BIO is discussing the matter with its members this week. The source says BIO's proposal has little chance

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Groups say affidavit requirement should at least be narrowed

FDA MAY ISSUE ANPR TO REVISE CONTROVERSIAL EXPORT MEASURES

FDA may issue an advanced notice of proposed rulemaking (ANPR) to revise two controversial requirements in a recent export notification and record-keeping rule: a requirement calling for firms exporting FDA-regulated products that may not be marketed in the United States to certify compliance with foreign law; and a provision stating that FDA can access food and cosmetics firms' export records. The agency has decided not to enforce these requirements as it considers whether to change them, according to sources and correspondence obtained by *FDA*

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FOOD, DRUG, DEVICE FIRMS BLAST CUSTOMS' PLAN TO TIGHTEN IMPORT LIMITS

Groups representing a broad spectrum of FDA-regulated industries strongly oppose a U.S. Customs Service plan to extend by six-months the time period during which an importer can be forced to return a product or pay a substantial penalty if FDA/Customs, decides the product violates FDA law. Customs' proposal would apply to drugs, food, devices and cosmetics.

Trade groups representing food, prescription and over-the-counter (OTC) drug, medical device and cosmetics makers are urging Customs' to either change or withdraw its June 7 notice of proposed rulemaking.

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receiver of the illegal prescription drugs before the agency may destroy or return them. The draft legislation would give FDA and the U.S. Customs Service the authority to detain any drugs that seem illegal and either send it back if a return address is provided or destroy the shipment, the source said.

At a House Energy and Commerce health subcommittee hearing two weeks ago, Rep. Bart Stupak (D-MI) had grilled FDA policy chief William Hubbard over the fact that the agency still had not submitted a legislative proposal to the House for stemming mail order reimportation. Stupak questioned why the agency had not followed up on a proposal made by Hubbard at a House Energy and Commerce Committee hearing 13 months ago.

Stupak was referring to Hubbard's testimony at a June 7, 2001, House Energy and Commerce oversight and investigations subcommittee hearing regarding concerns about imported pharmaceuticals. At the hearing Hubbard had said that FDA should be allowed to ask Customs to deny entry and return to sender all foreign pharmaceuticals arriving via mail. Hubbard said a proposal was at HHS, and if it was approved he would return to Congress with legislation to make the proposal a reality.

BROWN'S BILL ASKS FDA TO STUDY DRUGS REIMPORTED FROM CANADA

A key House Democrat's reimportation bill introduced just a day before the House broke for recess takes a different approach to the issue from other reimportation bills now circulating on Capitol Hill, according to a congressional source. Instead of requiring HHS to certify the program is safe before it is implemented, House Energy and Commerce health subcommittee ranking member Sherrod Brown's (D-OH) bill calls for FDA to study whether the program is safe after it has been implemented.

Brown's bill, which would only allow for personal reimportation, comes at a time when FDA is floating a legislative proposal aimed at curbing unsafe drugs brought into the country by mail (see related story).

The bill specifies that during the first year after the act becomes effective, the HHS secretary would conduct a study on the quality of drugs being reimported from Canada and other countries, the source says. The bill transfers the onus of responsibility from having to prove that the drugs are safe to having to prove that there is a problem with imported drugs, the source says, which is why it does not include a provision requiring the HHS secretary to certify that the imported drugs are safe.

[The full text of Brown's bill is available on *InsideHealthPolicy.com*; see page 5 for details.]

Until FDA conducts its study, the agency must permit individuals to buy or receive prescription drugs from Canada, the source added. If the analysis finds that there is a problem with reimported drugs then the HHS secretary may either impose conditions for reimportation in order to protect public health or bar individuals from importing drugs at all in order to protect public health.

FDA is not expected to like this new proposal, the source said, although there has been no official reaction from the agency. However, there is a possibility that FDA may like the idea of conducting a study of the program, the source said, because the agency has said before that if given the resources they would like to study the safety of drugs from across the border.

Supporters of this bill include Democratic Reps. Marion Berry (AR), Frank Pallone (NJ), Ted Strickland (OH) and Tom Allen (ME). The source added that Brown's office did not have time to shop the bill for support before the August congressional recess. While Rep. John Dingell (D-MI) has traditionally been opposed to the idea of reimportation, the source said the bill might get backing from some Republicans like Jack Kingston (GA) and Gil Gutknecht (MN), who have introduced their own bill on reimportation (see *FDA Week*, July 26, p3).

The source also said that Brown's office does not expect a markup on the bill because the GOP leadership will not consent to a markup on a Democratic bill. When the Kingston bill is marked up in September, Brown may consider supporting as is, or introduce amendments to add his own language to the bill.

New FDA Rules and Guidances

FDA is announcing the availability of a revised draft guidance for industry entitled "Potassium Chloride Modified-Release Tablets and Capsules: In Vivo Bioequivalence and In Vitro Dissolution Testing." This draft guidance provides recommendations to sponsors of abbreviated new drug applications on the design of bioequivalence studies for modified-release dosage forms of potassium chloride.

FDA is releasing a guidance document intended to provide a general description of FDA Export Certificates to industry and foreign governments. Firms exporting products from the United States are often asked by foreign customers or foreign governments to supply a certification relating to products subject to the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§321-397, and other statutes FDA administers.

Kennedy, Feinstein, Hatch cloning bill has more than 50 votes…
BROWNBACK MAY EYE MORATORIUM ON CLONING IF HE LACKS VOTES FOR BAN

Sen. Sam Brownback (R-KS) may be willing to support a moratorium on cloning research if he is unable to garner enough votes to pass his long-sought cloning ban, according to a congressional source. The senator is also considering a ban on the patenting of the process of human cloning and the products that are derived from it.

The senator has received indications that various backers might be more comfortable with a moratorium than a ban, the source says. Brownback may therefore back down on his call for a complete ban if there is the opportunity to get enough votes on the Senate floor to pass a moratorium, the source adds. The senator may be willing to consider a two- or three-year moratorium depending on the number of votes, the source added.

Banning the patenting of human cloning would mean that researchers would not be able to get patents on human beings from the one-cell zygote stage, the source said. While stem cell research would not be swept up by the ban, banning the patenting of the process of human cloning and the products that are derived from it would take away the financial incentives to continue cloning, another source close to the issue said. According to this source, "the incentive here is not cure, but rather profits." Therefore, when companies cannot commercially exploit the process of cloning, there is little motivation to do research.

Last month the President's Council on Bioethics voted in favor of a ban on reproductive cloning and a four-year moratorium on therapeutic cloning by a vote of 10 to seven with one member abstaining. While Brownback was "heartened" by the council's decision, Democratic senators backing another cloning bill were not pleased with the council's decision to endorse a moratorium on stem cell research. They were quick to note, however, that the council did not back Brownback's proposal for a complete ban on "critically important stem cell research."

T**he cloning bill introduced by Democratic Sens. Edward Kennedy (MA) and Dianne Feinstein (CA)** and Republican Sens. Arlen Specter (PA) and Orrin Hatch (UT) is moving closer to gaining the 60 votes it needs to pass the Senate. The source said that the bill already has the backing of more than 50 senators although "there is work to be done."

"This is the only bill that has a shot at passing," the source said, adding that the Kennedy-Feinstein bill also calls for a ban on the cloning of human beings. Some time ago, Senate majority leader Tom Daschle (D-SD) had promised Feinstein a floor vote if the bill managed the 60 votes it needs for passage. At press time, Feinstein's office could not confirm if the assurance still holds.

Hatch's backing on the bill was crucial for Kennedy and Feinstein since he might represent the swing vote that decides the type of cloning legislation that ultimately makes it through the Senate. Opponents of the bill say it does not provide regulatory control over therapeutic cloning. Moreover, they say it does not deal comprehensively and accurately with establishing a chain of custody for embryos, and establishing a system of egg donation and regulation preventing commodification of embryos (see *FDA Week*, Feb 8, p20).

Agency warns company of violations covering Meridia, other drugs
FDA INVESTIGATING ABBOTT OVER ADVERSE EVENT REPORTING FAILURES

FDA has launched an investigation into Abbott Laboratories over its repeated failure to properly report adverse events associated with Meridia and other drugs, and this week sent a warning letter to the company. A Public Citizen source said the investigation may lead to criminal charges and prompt FDA to finally withdraw the controversial diet drug Meridia from the market.

FDA's warning letter chides the company for not reporting a death possibly linked to Meridia, and for reporting another death late.

[The six-page warning letter can be found on *InsideHealthPolicy.com*; see page 5 for details.]

Many of the violations occurred at Knoll Pharmaceuticals before Abbott bought the company in March 2001. However, Abbott is responsible for Knoll's actions because the company is its subsidiary.

A former employee of Knoll Pharmaceuticals has gone to FDA as a whistle blower in a criminal probe against the company, according to a source from the consumer-interest group Public Citizen. The employee originally went to Public Citizen, but the group immediately referred him to FDA. The whistle blower, who Public Citizen would not name, is suing Knoll for allegedly firing him for complaining about the company's adverse event reporting problems. FDA's Chicago regional office, which sent the warning letter, declined to comment on whether a criminal investigation is underway, saying it is agency policy to neither confirm nor deny the existence of criminal probes.

After obtaining FDA's inspection reports, last May Public Citizen sent a strongly worded letter to HHS Secretary Tommy Thompson urging him to bring criminal charges against Abbott Laboratories for not telling FDA about a death associated with the company's weight-loss drug Meridia.

Two FDA inspections earlier this year found that in at least 18 cases the company was late in submitting serious and unexpected adverse drug experience reports within 15 days of discovering the problems, according to the letter.

Instead the company incorrectly categorized these reports as periodic adverse drug experience reports, which FDA requires be submitted quarterly for three years following a drug's approval.

In several instances, the company also failed to submit follow-up reports with 15 days of receipt of new information or as requested by FDA.

In the case of Meridia, Abbott told FDA that Knoll had reported all events that met the reporting criteria required under law. Knoll said an unidentified person called the company to report a death the person believed was due to Meridia. The company deemed the call a rumor, which it says it did not need to report to FDA.

FDA disagrees, saying Knoll still was required to report the death.

In seven deaths caused by Meridia, the company failed to maintain records of raw data and correspondence in follow-up investigations.

In other instances Knoll lied in reports to FDA, according to the warning letter. For example, the company reported that an autopsy of someone who died after using Meridia found nothing. But the company's own records state "autopsy did not reveal anything other than left ventricular hypertrophy."

Other drugs involved in the reporting violations include Norvir, Biaxin and ProSom.

TRADE GROUPS STILL MEETING ON DEVICE USER FEE . . . begins on page one

source declined to explain what the limitations are. In order for MDMA to agree to a user-fee plan, it must have some sort of a tiered approach for PMAs that charges smaller companies less than large companies.

A spokesperson for the Advanced Medical Technology Association (AdvaMed) says he is not aware of a member vote on a legislative proposal. He also says AdvaMed has not seen any MDMA proposal.

[An MDMA proposal from earlier this week before congressional staffers proposed the compromise plan can be found on *InsideHealthPolicy.com*; see page 5 for details.]

"There are no changes to the AdvaMed proposal," the spokesperson said, referring to a user fee deal struck in private between AdvaMed and FDA last May.

Under the FDA-AdvaMed plan, companies would pay $125,000 per PMA during the first year, irrespective of company size. Companies would pay $25,000 for PMA supplements and $2,500 for 510(k)s. Fees would increase annually over the five-year period.

The FDA-AdvaMed plan also aims to allow small companies to make money from a device before paying the fees. Under the plan, small device companies — companies claiming $5 million or less on their last federal tax filing – could defer payment for a year after FDA makes a final decision to approve the device.

MDMA rejects this provision. The group says many companies don't make any money from a new product for up to five years following approval.

In order to curb the higher administrative costs of managing a two-tiered approach, MDMA is pushing a system that would require a company's chief executive to claim the size of his company on FDA applications. Stiff penalties would keep executives from lying.

Congressional staffers have been trying to broker a deal between MDMA and AdvaMed. The two trade groups, which strongly oppose one another's position, are resuming negotiations with congressional and FDA staffers today (Aug. 9), according to the MDMA source.

Staffers became fed up with the trade groups earlier this year after negotiations failed and started working directly with device companies on device reforms, according to a congressional source. There are three legs to the legislation: user fees, third-party inspections of manufacturing plants, and stricter labeling for reused devices, according to congressional and industry sources.

The user fee part of the proposal must be worked out between the two trade groups, but congressional staffers want to finish the negotiating by as early as the end of next week, MDMA sources say. It is unclear if staffers have worked out an agreement on reused device labeling or third-party inspections. Sources say the one provision that most people can agree on is the creation of a combination product office.

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HOUSE ENERGY & COMMERCE TO HOLD SEPT. DRUG PATENT REFORM HEARING

The House Energy and Commerce Committee plans to hold a hearing on drug patent reform sometime in September, according to a Democratic staffer. This is good news for several House Energy and Commerce Committee Democrats who recently urged committee chairman Billy Tauzin (R-LA) to schedule a hearing on House drug patent reform measures after the August recess.

House Democrats and Republicans recently introduced patent reform bills that closely resemble the bill passed by the Senate July 31. Until recently it appeared that the House would not move forward on patent reforms.

Tauzin's plan to hold a hearing will likely prompt strong lobbying by the supporters and opponents of the Senate legislation over the August congressional recess.

The pharmaceutical industry strongly opposes the Senate bill.

The biotechnology industry also recently got involved in the fray after discovering a last-minute addition to the Senate bill that could potentially create a pathway for FDA to approve generic biologics. To the biotech industry's dismay, the controversial bioequivalence provision was also included in the recently introduced House bills.

The Biotechnology Industry Organization (BIO) plans to work hard to get the provision removed. BIO thought it had reached a deal with Senate lawmakers to change the provision before the Senate passed the bill, but alternative language inserted by Senate health committee chairman Edward Kennedy (D-MA) did not assuage BIO's concerns.

A BIO source says a BIO-spearheaded grassroots effort will target certain members in the districts over the congressional recess. BIO hopes to educate members about its opposition to the bioequivalence and other provisions in the House and Senate bills.

On the opposite side of the issue, the Generic Pharmaceutical Association (GPhA) will be lobbying key members both inside and outside the beltway to support House passage of patent reform legislation.

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- FDA Sends Warning Letter To Abbott Labs Complaining It Violated FDA's Adverse Reporting Requirements
- AMA Urges Senate Panel To Prohibit Marketing Of Dietary Supplements Containing Ephedrine Alkaloids
- Armey Manager's Amendment Includes Provision Allowing Companies That Make Counterterrorism Products To Apply For Liability Indemnification
- Bush Administration Proposes Updated Field Testing Requirements For Biotechnology Derived Foods
- FDA Seeks Input On Gene Therapy, Public Meeting Scheduled For Sept. 9
- MDMA Floats Device User Fee Plan: Large Firms Would Pay $150,000 Per PMA, Small Firms Would Pay $37,500
- CRS Updated Report For Congress Investigating The Ethical And Moral Issues On Human Cloning
- Alabama Implements New Bulk Purchasing Law And Urges Congress To Reform Drug Patent Rule
- The Association of Food and Drug Officials Asks FDA For A Meeting To Discuss How AFDO Can Re-energize Its National Food Safety System
- FDA Issues Guidelines For Its Staff When Reviewing Combination Products
- CBER Issues SOPP Manual On Processing Biologics License Application Supplements
- OMB Issues Final Guidance For Implementing The 'Select Agent Registration' Provision Of The Recently passed Bioterrorism Law
- Brown Introduces Reimportation Bill Authorizing HHS To Provide Waivers To Persons Importing Rx Drugs From Canada
- CSPI Letter To FDA Urging A More Prominent Olestra Warning Label On Snack Food Packages
- Food, Drug And Device Firms Oppose Customs' Plan To Tighten Import Limits
- FDA Won't Be Pressured In Its Olestra Labeling Decision

KENNEDY FLOATS AMENDMENT TO MANDATORY ALLERGEN LABELING BILL

In a bid to appease Senate GOP concerns, Senate health committee chair Edward Kennedy (D-MA) is floating a substitute amendment to his bill that would make food processors list allergens in common language. Although Republicans have indicated that the amendment is a move in the right direction, they say the amendments still do not do enough to alleviate their concerns.

Among other changes, the substitute amendment would eliminate a section that would establish civil monetary penalties, would extend the amount of time companies have to comply with the new labeling requirements, eliminate a requirement that FDA promulgate good manufacturing practices (GMPs) regulations aimed at reducing cross-contamination and eliminate a provision under which a product could be misbranded if the food label says a food "may contain" a particular allergen, according to the congressional source and food industry sources.

The Center for Science in the Public Interest (CSPI), which helped write the original legislation, does not have a position on the amendment, according to a CSPI source. However, the CSPI source reiterated the need to pass legislation to force food companies to label allergens in clear language.

One food industry source states that the amendment appears to go in the right direction by eliminating the civil monetary penalties and giving industry more time to comply. Under the original bill, the labeling requirements would go into effect 180-days after enactment. Under the amendment floated by Kennedy, companies would have until Jan. 1, 2004 for products that contain allergens and until Jan. 1, 2005 for foods that do not contain allergens.

But the food industry source says that even though the amendment goes in the right direction, the food industry continues to oppose the bill on the grounds that a mandatory approach is not appropriate or needed, and that instead the food industry should be allowed to continue to implement its voluntary guidelines.

Another food industry source is more critical of the amendment, arguing that while certain aspects of the bill go in the right direction, other aspects of the amendment actually make things worse. Under the amendment, instead of putting in bold the common name of the allergen the firm would have to put an asterisk next to an allergen or intolerance. The food industry source says that this would broaden the scope of the bill.

However, a congressional source says that this is not the effect of this provision. The provision was simply trying to better characterize gluten, something that both the original bill and the amendments require to be labeled, the source says. Critics of the bill had charged that scientifically, gluten is an intolerance not an allergen.

The food industry source also objects that under the original bill, if the allergen was already labeled in common language, the firm would not have to change the label. This is no longer the case under the amendment. The food industry source says there are also concerns about a new misbranding provision that industry lawyers read as requiring the labeling of spices, flavorings, colorings and incidental additives that contain any food allergen — where the rest of the bill talks about labeling for known allergens.

S. 2499, "The Food Allergen Consumer Protection Act of 2002," as introduced by Kennedy, would require products to list in bold face type the common or usual name any of the eight main food allergens (milk, egg, fish, Crustacea, peanuts, tree nuts and soybean), proteins derived from those substances and other glutens such as rye, barley, oats, and triticale.

PEDIATRIC GROUPS URGE TAUZIN STAFF TO BACK PEDIATRIC RULE CODIFICATION

Pediatric advocacy groups are pressing House Energy and Commerce Committee chair Billy Tauzin (R-LA) to champion a House version of a bill that would codify a rule allowing FDA to require companies to study the effects of their drugs and biologics in children, according to a pediatric source. Pediatric advocacy groups met with Tauzin's staff Aug. 5.

Just before the Senate left for its August recess, the Senate health committee unanimously passed a bill introduced by Sens. Hillary Clinton (D-NY), Mike DeWine (R-OH) and Christopher Dodd (D-CT) that would codify the pediatric rule. Senators worked out a compromise that would prohibit FDA from forcing companies to conduct pediatric studies on already-marketed drugs until after FDA offers the company six months of market exclusivity (see *FDA Week*, Aug. 2, p1).

Pediatric advocates hope to galvanize the House Energy and Commerce Committee into passing a similar bill. The legislative proposal has strong support from committee Democrats, but currently no Republicans are on board. Committee member Henry Waxman (D-CA) introduced H.R. 4730, the House companion bill. The bill is cosponsored by committee ranking Democrat John Dingell (MI) and health subcommittee ranking Democrat Sherrod Brown (OH), as well as Democratic Reps. Rosa DeLauro (CT) and Anna Eshoo (CA).

The pediatric advocates are working to get GOP members on board. The groups hope to persuade Tauzin to cosponsor the bill and to "act as a catalyst" to move the bill through the committee. As a preliminary step towards this goal, the pediatric groups recently met with Tauzin's staff.

The source says that the questions posed by Tauzin's staff suggested a reluctance to impose requirements upon industry. The pediatric groups argued that the bill is narrow in scope. They pointed out to Tauzin that the legislation would not require drug firms to conduct studies for off-label indications, and provides for deferrals and waivers of certain pediatric subpopulations, according to the source.

The groups also told Tauzin that the bill would not establish new policy. But the groups feel that the bill is necessary in light of the current lawsuit challenging the pediatric rule, and the Bush administration's attempt earlier this year to get the courts to stay the pediatric rule for two years to give the agency time to review it. The agency quickly dropped its request to stay the regulation in the wake of criticism from both those who support and oppose the rule. Among those most critical of FDA's attempt to stay the rule were House Democrats, who support the rulemaking.

OHRP WORKING GROUP FOCUSES ON QUALITY IMPROVEMENT TOOLS FOR IRBs

An unofficial expert panel convened by the Office for Human Research Protections (OHRP) is providing input on how best to develop quality improvement (QI) techniques that OHRP can apply to Institutional Review Boards (IRBs), according to an expert on human subject protection.

OHRP's QI program was launched earlier this year to help institutions evaluate and improve the quality of their human research subject protection program. It aims to increase the quality, performance and efficiency of an institution's human subject protection program and includes three stages: 1. quality assurance; 2. quality improvement; and 3. continuous quality improvement.

While the first stage focused on helping IRBs attain compliance with federal regulations, the meeting on Tuesday (Aug. 6) launched the second stage of the QI program — to help IRBs improve the quality of their reviews, according to a government source.

The panel comprising experts from OHRP, FDA, accrediting bodies, private and independent IRBs and academia discussed mechanisms by which OHRP can measure the performance and quality level of IRBs, the source said. Following regulations raises the quality level of an IRB and it is a sound base on which the quality of review can be improved, the source said.

Experts are looking at ways to develop a program or system by which OHRP can interact with the IRBs to help improve the quality of their review, the source said. Calling the meeting a success the source said those present were brainstorming to gain an impression of which direction to take, what type of products to focus on, and were trying to answer questions about whether quality improvement needs to focus on specific areas of research or not.

The difficult aspect of the task, the source said, is that measuring quality is challenging, because quality is difficult to quantify.

OHRP is focusing on being able to review the decision-making process of IRBs, the source said, and is concerned with the process of decision making and examining how the IRB looked at minimizing risk to the subject. The last few years, the source said, have seen a doubling of IRB loads due to increased NIH funding for human research and this has shaken the trust in the IRB review process. According to an expert in human subject protection, the timeliness of reviews, the amount of information an IRB shares, with whom and how much, the training of IRB members and staff are all questions that need to be considered when evaluating the quality of an IRB's review process.

FDA is an invited participant in this effort, the government source said, The next meeting may be scheduled sometime during fall.

ACLU: FDA'S DTC PRINT ADS ARE TOO RESTRICTIVE OF COMMERCIAL SPEECH

The American Civil Liberties Union (ACLU) says FDA's direct-to-consumer (DTC) print advertising practices overly limit commercial speech and is urging the agency to extend its broadcast model to print ads. The free-speech group also suggests FDA use methods other than speech restrictions, such as requiring a doctor's prescription for certain dietary supplements, to protect consumers from potentially harmful effects.

"For example, [FDA] could require a doctor's prescription for both dietary supplements and drugs that are powerful or have dangerous side-effects. This would promote public health by providing additional guidance and monitoring to consumers without restricting speech," the group states in recent comments to FDA.

ACLU maintains that FDA should base its restrictions on the potential risk posed by the substance, no matter whether that substance is classified as a drug or a dietary supplement. "Both drugs and dietary supplements affect the body and should be treated according to the level of danger they pose rather than what type of product they are," ACLU argues.

ACLU is making recommendations on FDA DTC advertising practices and other commercial speech issues in response to the agency's call for input on whether its regulations and guidances comply with the First Amendment. [The comments are available on *InsideHealthPolicy.com*; see page 5 for details.]

The group is particularly upset by FDA's requirement that print ads include a brief summary. The prominent civil liberties group says that due to FDA's brief summary requirement, DTC print ads may be too dense for consumers to understand. "Though the regulation of DTC advertisements requires a 'brief summary,' print advertisements for prescription drugs contain almost as much information: The advertisement must list side effects, warnings, precautions, and contraindications that the drug's labeling contains. Therefore, the resulting advertisement for consumers' eyes is almost as technical and difficult to read as that intended for medical professionals," the group states.

The agency requires that print advertisements contain a brief summary of all the drug's risks. For DTC print ads the agency allows drug firms to rewrite the package insert so that the information is more consumer-friendly, according to a source familiar with the topic. However, the brief summary must include all risks, and some of those risks are extremely difficult to translate, the source says.

"[I]t has taken some steps in the direction of revision by issuing its consumer-directed broadcast advertisements guidance in 1999 and a draft guidance for industry permitting use of FDA-approved patient labeling in consumer-directed print advertisements in 2001. However, since then, if has not taken further steps in the right direction," the group states.

The group suggests the agency apply its DTC broadcast advertising policy to DTC print advertisements as a possible solution that would allow the agency to accomplish its goals in the least-restrictive manner possible.

Broadcast advertisements can omit the brief summary if adequate provisions are made to disseminate the risk information to consumers. The agency's 1999 guidance paved the way for a huge increase in DTC broadcast advertising, according to a food and drug lawyer, by laying out what a drug firm would have to do to make adequate provisions to distribute the risk information. It would be extremely difficult for a broadcast ad to include the brief summary, but prior to the 1999 guidance drug firms were hesitant to advertise because the provision was ambiguous, the source says.

A source closely following the issue says there is merit to the idea that FDA follow a similar approach for DTC print ads that it does for broadcast ads by allowing drug firms to put just the most-important risks in the actual copy if the drugmaker ensures that the consumer can find the more-detailed risk information somewhere else, such as by calling a 1-800 number.

"Alternatively, it [FDA] could require that the 'brief summary' be more 'brief,' and be made more comprehensible to the ordinary consumer. ACLU recommends finally, it could take the initiative in proposing that the industry propose and adopt its own standards regarding a clearer and shorter format for print advertisements."

FDA MANUAL OUTLINES BASIC RULES FOR COMBO PRODUCT COLLABORATION

FDA's recently released manual of standard operating procedures lays down basic procedures that various centers should follow when collaborating for reviews on combo products that experts say are long overdue. The document, which is the first of its kind, outlines basic rules for collaboration and by its own admission does not establish standards for when a consultative or collaborative review is required.

[The Manual of Standard Operating Procedures and Policies – Intercenter Consultative/Collaborative Review Process is available on *InsideHealthPolicy.com*; see page 5 for details.]

An agency official says this manual, released on Aug. 2, attempts to address and make clear the agency's policy on collaborative reviews. The manual, the agency source says, clarifies that deadlines for collaborative reviews are as important as regular deadlines by having the center directors set aside staff to do consultations. While the manual

explains that consulting reviewers should receive credit for timely reviews, it specifies that the progress of consulting reviews should be tracked by each centers' tracking system.

The manual also recognizes the need to set up a centralized method for monitoring the progress of Intercenter collaborations and states that future revisions will tackle that issue. The source said that the agency is looking into what needs to be developed to have a system in place that would be able to identify which combination products are under review and the time frame for each review.

As an outside expert in the field said, "the agency is not yet stepping into the quagmire of who should be in control for which product." Some other big questions as yet unanswered are: When does this manual need to be used? When should this manual not be used? and, Who decides when it is to be used?

News Briefs

COURT SAYS CLARITIN METABOLITE PATENT IS INVALID

At press time the U.S. District Court for the District of New Jersey ruled that a patent Schering-Plough listed in the Orange Book as protecting against generic competition of allergy drug Claritin (loraditine) is invalid because the patent is for a metabolite that naturally occurs when a person takes Claritin and was "anticipated by the patent" on Claritin. The metabolite patent, according to a source closely following the issue, is the active ingredient in Clarinex.

FOOD GROUP: FDA DOESN'T HAVE RIGHT TO SEE RECORDS . . . begins on page one

Week.

FDA announced that it was considering issuing an ANPR on these two issues and would continue to hold off enforcement in a July 22 letter to Covington and Burling lawyer and former FDA chief counsel Peter Barton Hutt. In an earlier June 20 letter to Hutt, the agency promised to delay enforcement of these two provisions until after July 19 in response to Hutt's June 17 letter asking the agency for a stay on behalf of the Grocery Manufacturers of America and the Cosmetics, Toiletry and Fragrance Association.

Hutt and a representative of one of the groups met FDA chief counsel Daniel Troy and other representatives of the Office of Chief Counsel on July 10 to discuss these two provisions and sent a follow-up letter on July 16, according to sources.

Although the agency has not yet publicly released the July 16 letter, sources say Hutt's letter states that the groups might be willing to provide an affidavit that a food or cosmetic export meets foreign laws, but only in cases where the export does not meet a U.S. safety or health requirement imposed to prevent a serious health risk.

For instance, sources say that Hutt suggests in the letter that an affidavit that the company is in compliance with foreign law could be required if FDA has established a warning label, or limited the amount of a particular substance could be in food or cosmetics because of a serious health risk, and the company does not adhere to those requirements. A possible example, according to a source, is aflotoxin, a naturally occurring mold that is thought to be carcinogenic and for which a limit has been established for food products.

This would not include the food additive limits, as these are not established because of food safety concerns, according to a source closely following the issue.

The contested final export and notification rule requires firms to prepare a notarized certification by a responsible company official that an exported product does not conflict with the laws of the importing country. In his June 17 petition for reconsideration and stay of action, Hutt said that the legislative history of the section demonstrates that Congress intended for FDA to bear the burden of proving that the shipment is not okay in the recipient country, and that companies should not bear the burden of showing the opposite.

[The June 17 letter is available at *InsideHealthPolicy.com*, see page 5 for details]

In the June 17 petition, Hutt maintained that the requirement that firms demonstrate that the product does not violate foreign law would have adverse impacts on food and cosmetic companies, who often label products in the United States in foreign languages, before export, in order to meet foreign requirements.

"The new provision would require the preparation of thousands of affidavits just for shipping products to our neighbors in Mexico (Spanish labeling) and Canada (dual French and English labeling), and new affidavits would be required for every product variation and every label change. FDA has presented no evidence that the approach used for the last 64 years has in any significant way harmed foreign consumers or relations between the United States and our trading partners," the June 17 petition argues.

Although Hutt only asked to stay the certification provision for the food and cosmetic industries, the agency stayed the provision for all FDA-regulated products that would be affected by the requirement, including devices

and drugs. In the July 22 letter, the agency is now extending that stay. The agency is also extending the stay on the provision under which the agency would have access to a food or cosmetic company's export records.

Sources closely following the issue say that although the food and cosmetic industries tried to reach a middle ground with FDA on the certification issue, middle ground cannot be reached on the records access issue. FDA does not have the authority to access records, according to industry sources. The agency may have the power to require food firms to keep records, but they do not have the authority to access those records, the sources say.

FDA NOT PRESSURED BY CONSUMER FOOD GROUP IN OLESTRA LABEL DEBATE

As the six-year-old debate continues over whether labels on foods containing the fat-substitute Olestra should contain warnings about health effects, FDA is refusing to be pressured by a consumer group to chide Procter & Gamble for not reporting consumer health complaints since last year.

In an April 16 letter to FDA, Center for Science in the Public Interest (CSPI) Executive Director Michael Jacobson hoped to pressure the agency into taking action against Olestra manufacturer Procter & Gamble for not submitting consumer complaints concerning a controversial fat substitute. But FDA refuses to be pressured, citing new studies that refute CSPI's claims that Olestra causes adverse health reactions.

According to a June 28 response letter, FDA is considering a Procter & Gamble petition requesting the removal of the Olestra warning label from popular snack food packages. This response comes in the midst of a six-year struggle by the consumer group to ban this popular fat substitute from the market.

[Both letters are available at *InsideHealthPolicy.com*, see page 5 for details.]

Olestra is a non-digestive fat substitute that was approved by FDA in 1996 under the following conditions: 1. that Procter & Gamble conduct a report on food products containing Olestra 30-months after appearing on the market and 2. that an informational label, "OLESTRA MAY CAUSE ABDOMINAL CRAMPING AND LOOSE STOOLS. OLESTRA INHIBITS THE ABSORPTION OF SOME VITAMINS AND OTHER NUTRIENTS," be placed on snack food packages containing Olestra.

Olestra soon became a popular substitute in fat-free snacks, the most popular being Frito-Lay's Wow! chips and Procter & Gamble's fat-free Pringles. Soon after Olestra appeared on the market, consumers started to file complaints of gastrointestinal discomfort after eating snack foods containing Olestra. Complaints were wide ranging — including cramping, bleeding, and chronic diarrhea. Although most symptoms were mild, "causing more embarrassment than harm," according to CSPI releases, some severe cases required hospitalization or surgery.

CSPI attacked Olestra after conducting a clinical study that confirmed consumer complaints that Olestra was causing loose stools or "severe" diarrhea in its participants.

In June 1998, the conflict seemed to fade during an FDA Food Advisory Committee (FAC) meeting where a majority of members supported the removal of the informational label. CSPI and Procter & Gamble agreed to submit consumer complaints in quarterly reports to FDA. CSPI's last report was issued on April 16, 2002, bringing the grand total of consumer complaints close to 20,000 — more than all other food additive complaints in history combined, according to an April CSPI press release.

In an April 16 letter, CSPI charged Procter & Gamble with failure to submit its quarterly reports to FDA. It was confirmed that Procter & Gamble had not honored its agreement for more than a year, sending its last report in January 2001. In addition, CSPI urged FDA to press Procter & Gamble to challenge previous Olestra studies by conducting their own tests.

FDA told CSPI that P&G has in fact contacted a number of consumers who had filed complaints about Olestra and submitted them to a double-blind placebo test. Half of the participants were given food-containing Olestra and the other half was given food without Olestra. Procter & Gamble reported that none of the participants reported any adverse reactions to the fat substitute. CSPI doesn't think FDA should consider Procter & Gamble's report because it doesn't think the company's study used enough people over an appropriate length of time.

"We stopped sending reports to FDA because the number of complaints had gone down and it was the same stuff we had been hearing all along," the Procter & Gamble source says.

Although CSPI admits that it is still unclear under what conditions Olestra causes adverse reactions (i.e. time, what foods it is mixed with, etc.), it has extended its fight to include an all-out ban of Olestra.

"We are still opposed to Procter & Gamble's petition [to remove the informational label from snack foods]," a CSPI source says. "We want Olestra removed from the market completely."

Procter & Gamble will continue to press FDA to remove the information label from Wow! and fat-free Pringles packages because, according to the Procter & Gamble source "Olestra doesn't affect the body any more than life does."

FDA is now reviewing all materials concerning Olestra and is expected to make a decision on the fat substitute's label future some time in the near future.

"We expected stool softening from the start," A Procter & Gamble source says. "The information label was a precautionary measure because Olestra is non-digestive and needs to be released from the body like anything else."

The groups charge that the notice of proposed rulemaking substantially departs from Customs' current practice, establishes an excessively long "conditional release period," fails to provide a good reason for the significant change, will not help FDA food safety efforts, will impose an economic burden on importers and is impractical.

Several food groups add that food can rot during such a long period, the terms of the proposed conditional release period are not clear and the proposal violates the Regulatory Flexibility Act, an Executive Order and international trade agreements.

Under current law, if the importer posts a bond Customs can release goods to the importer on a conditional basis while FDA considers whether they can be admitted. Currently, Customs and FDA must get back to the importer in 30 days or forfeit their right to collect the bond.

The Customs notice of proposed rulemaking would establish a 180-day "conditional release" period for all imported food, drugs, medical devices and cosmetics. Moreover, under the proposal, Customs would have up to 30 days beyond the end of this 180-day conditional release period to demand "redelivery" of FDA-regulated merchandise in cases where FDA determines, at any point during the 180-day period after the initial release of the merchandise from Customs to the importer, that the merchandise should not be allowed into the country.

If the importer refuses to redeliver the goods, that refusal will be considered a breach of the mandatory Customs bond. The importer would have to pay liquidated damages of up to three times the value of the goods or its domestic retail value, whichever is higher.

The normal Customs practice, according to Aug. 6 comments submitted by law firm Collier Shannon Scott on behalf of several food groups including the Grocery Manufacturers of America, is that the release of goods to the importer is conditional during the first 30 days. Customs has the right to demand redelivery during that time.

[Collier Shannon Scott's comments can be found on *www.InsideHealthPolicy.com*; see page 5 for details.]

Currently, after that initial 30-day period, unless the period is extended either by regulation or by an action taken by Customs or FDA that indicates interest in the import, if Customs asks for the product back, the importer cannot be charged a penalty if it does not return the goods.

Under current practice, agency actions that are regarded as extending the normal 30-day conditional release period if taken before the close of the 30-day period include a CF 28 request for information or sampling, a CF 3461 stamped with an FDA notice of sampling, or an FDA notice of detention, according to Collier. Collier faults a series of headquarters rulings holding that the failure of FDA to issue a "may proceed notice" counts as an affirmative action that would trigger an extended conditional release policy.

Under the June 7 notice of proposed rulemaking, Customs could demand importers return the product or pay penalties up to 30 days after the conditional release period — for a total of 210 days.

The trade associations argue that the 180-day period is an excessively long time for Customs to be able to demand that an importer return the product or pay an expensive penalty. This long period creates logistical problems for the importer, according to the groups.

The National Food Processors Association (NFPA) states that the 180-day time period is unreasonable and inappropriate. "Food importers cannot set aside raw materials for over six months while safety and quality deteriorate, storage costs mount and working capital is swallowed up. Nor can food manufacturers afford to gamble on a possible redelivery order for which failure to redeliver the merchandise will result in liquidated damages equal to three times the value of the merchandise," NFPA argues in its Aug. 6 comments.

[NFPA's comments can be found on *InsideHealthPolicy.com*; see page 5 for details.]

Customs needs to take into account the fact that foods may perish, according to NFPA. "A large quantity of food imported into the U.S. and inspected at port of entry under the authority of the Food and Drug Administration (FDA) is highly perishable raw fruits and vegetables either for retail sales or further processing. These products would be unusable after six months; it would be impossible to recall or recondition the products after that time," the group maintains.

Processed foods are also usually consumed within six months, NFPA adds. "[E]ven the most shelf-stable foods may have some quality deterioration if held for a six-month period. For example, flavorings, seasonings, coffee and negative taste attributes," the group states.

The Consumer Healthcare Products Association (CHPA) argues that the rule puts firms in a difficult position as tracking the products for that long would be difficult, and holding the product for that time period is not a palatable option. "The proposed rule's imposition of a conditional release period of 180 days would effectively place products in a limbo for up to seven months — a period which can be well beyond that in which the manufacturer has control over the product. In contrast, if manufacturers were to ensure that components or products were held for that length of time, it would necessitate significant changes in storage, warehousing logistics, and facilities," the group maintains in its Aug. 2 comments.

[CHPA's comments can be found on *InsideHealthPolicy.com*; see page 5 for details.]

The six-month time period is also unreasonable for devices, according to the Advanced Medical Technology

Association (AdvaMed), and could make a large number of imported products unusable. A lengthy detention could result in delayed shipments and back orders, and product waste, the group adds. "Many products have only a one-year shelf life. More than half of the product life could be lost awaiting FDA clearance. Other products may require special handling, particularly those used for research. Extensive delays would compromise these materials and any associated medical research," the group states in Aug. 6 comments.

[AdvaMed's comments can be found on *InsideHealthPolicy*.com; see page 5 for details.]

Law firm Barnes, Richardson and Colburn sent in an Aug. 6 one-page "placeholder" submission to Customs on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA) highlighting the group's preliminary concerns. On Aug. 2 PhRMA requested a 30-day extension to prepare comments, however this request was denied. But Customs suggested that as long as the association got something in by the deadline, it might consider a more fleshed-out document at a later date, according to a PhRMA spokesperson. The group intends to submit a more comprehensive document in the next couple of weeks.

In the placeholder document, the law firm states that although the group is continuing to gather input from its members to gather a more comprehensive response, the group has concerns with the proposal. "If a new regulatory limitation is to be established on the use of redelivery procedures by Customs the proposed 180 day conditional release period is too long," according to PhRMA.

Several groups argue that Customs has not provided a convincing reason for the proposal, adding that the rule will not help FDA with its enforcement efforts. Customs says the plan would "provide a reasonable period of time to allow FDA to perform its enforcement functions." However, the groups maintain that the rule would do little to help ensure food security.

PhRMA states that Customs has failed to provide a rational basis for proposing this definitive conditional release period.

AdvaMed agrees with PhRMA that the rule is not needed to help the agency achieve its enforcement goals. "The NPRM [notice of proposed rulemaking] states that the purpose of extending the conditional release period is to allow FDA to perform its enforcement functions. According to the proposed rule, FDA could take as long as six months to make a decision on whether or not to issue a 'may proceed' on imported merchandise. The medical device industry has seen little or no indication that the current 30 days is not sufficient for FDA to perform its enforcement functions," AdvaMed states in its Aug. 6 comments.

Several of the food groups go so far as to argue that the plan would contravene FDA's enforcement efforts. "If it takes the agency 180 days to determine whether a food, drug or medical device appears to be adulterated or misbranded, it is not fulfilling its mandate to protect the public from unsafe or mislabeled goods," Collier's comments state.

Collier continues: "The proposed rule perpetuates delays in admissibility determinations, rather than instill a sense of urgency to promptly inspect and prevent harmful goods from entering the United States. To the extent that the proposed rule is designed to allow FDA to interdict unsafe merchandise, it is obvious that a shorter — rather than a longer — release period is essential to effectuate the agency's mandate."

Some of the groups maintain that Customs does not take into account new efforts geared at protecting against tampering the food supply. NFPA urges Customs to consider regulatory changes regarding prior notice. For instance, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 mandates new regulations requiring prior notice for entering food products. "NFPA urges U.S. Customs to postpone any further action on this regulatory proposal until the implications of all expected procedural changes at port of entry can be considered concurrently. In this manner, the burden to food importers and enforcement agencies can be minimized, while security gaps are closed," the group states.

The food groups call on Customs to conduct an initial regulatory flexibility analysis of the proposed rule. In a July 31 letter, a group of food associations and companies largely matching the groups represented by Collier urged Customs to rescind the proposed rule on the grounds that the notice of proposed rulemaking fails to comply with the Regulatory Flexibility Act and Executive Order 12866.

Although the agency denied the July 31 request, the food groups represented by Collier say Customs is required by 5 U.S.C. section 603 to perform a regulatory flexibility analysis. "The agency may not simply dispense with the required analysis by reciting, without support, that the 'proposed amendments, if adopted, will not have a significant economic impact on a substantial number of small entities.' The full analysis should be made available to the public and shared with the Small Business Administration, as required by the RFA," the groups maintain.

In accordance with executive order 12866, the Office of Management and Budget should review the rule, according to the food groups, as the proposed regulation "clearly constitutes 'significant regulatory action' within the meaning of the Executive Order."

At press time comments from the Cosmetics, Toiletry and Fragrance Association had not yet been obtained by *FDA Week*.

OMB approves data-collection provision of bioterror law...
EVEN LABS WITHOUT SELECT BIOLOGIC AGENTS MUST REGISTER WITH CDC

The Office of Management and Budget (OMB) has approved a plan implementing a recently passed law requiring laboratories in possession of select biological agents, such as smallpox, to report the agents to the government. Under the data-collection plan even facilities without such agents must submit a declaration of nonpossession so the government knows of laboratories that could possess them in the future.

Laboratories have little time to report. The law requires those possessing "select agents" to notify the Centers for Disease Control and Prevention (CDC) by Sept. 10. "High consequence livestock pathogens or toxins" are to be reported to the U.S. Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) by Oct. 8, 2002.

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 lists the pathogens the government plans to track. [The OMB-approved plan is available on *InsideHealthPolicy.com*; see page 5 for details.]

CDC and APHIS are sending out the guidance document and form to about 190,000 facilities. Both use a common notification form, which labs should receive by Aug. 16.

The CDC received several comments on five main topics: definition of facility, exemptions, notification of nonpossession, the time to fill out the form, and the select-agent list.

According to the OMB notice, CDC is defining a facility as "any individual, or government agency, university, corporation, company, partnership, society, association, firm or other legal entity located at a single geographic site. A single geographic site is a building or complex of buildings at a single mailing address."

CDC says that although Congress discussed the possibility of exempting certain laboratories from the law, lawmakers rejected any broad exclusion for these facilities. The law exempts registration of clinical and diagnostic laboratories "only if they report the identification of select agents to the [HHS] Secretary and either promptly transfer the agent to a registered person or destroy the agent on site in accordance with regulations established by the Secretary.''

The congressional conference report further explains that laboratories that use select agents for reference purposes must register and be subject to regulatory program. Although such laboratories must participate in this initial notification phase, HHS and USDA are supposed to develop regulations allowing exemptions for laboratories that "only possess, use, or transfer select agents contained in specimens presented for diagnosis, verification, or proficiency testing." For now, CDC and APHIS are requiring all clinical and diagnostic laboratories that possess any listed agent or toxin to submit a form.

Although many who commented were concerned that CDC is underestimating the amount of time respondents will need to fill out the forms, CDC is still estimating that on average it will take two hours to review the instructions, gather the data, and complete the form.

BIO MEMBERS DISCUSSING INDEMNIFACTION PLAN . . . begins on page one

with the caps included because trial lawyers hate the idea. Last year, the Association of Trial Lawyers of America thwarted BIO efforts to gain congressional and White House backing to shield vaccine makers from liability as part of the recently enacted bioterrorism law (see *FDA Week*, Nov. 16, p1).

If BIO were to agree to a removing the caps, it's proposal would resemble the indemnification amendment offered by Rep. Jim Turner (D-TX) just before summer recess. The trial lawyers did not oppose Turner's amendment. The House defeated by one vote the mostly Democrat-backed amendment in favor of an indemnification provision in Rep. Dick Armey's (R-TX) manager's amendment. The Bush administration also lobbied against the Turner amendment (see *FDA Week*, Aug 2, p1).

[The Turner amendment and the House-passed indemnification language are available on *InsideHealthPolicy.com*; see page 5 for details.]

House Democrats and trial lawyers say Armey's indemnification provision is too broad. The House-passed bill would expand current government-contractor immunity to other companies that apply for such immunity. The version included in the House-passed bill would prohibit plaintiffs from seeking punitive damages that are not intended to compensate for actual losses. Under the provision, plaintiffs could only claim noneconomic damages directly proportional to a company's percentage of responsibility.

However, for younger companies such as those found in the biotech industry, the Armey amendment is too narrow, according to the BIO source. Defense manufacturer Lockheed Martin is behind the language, and it requires that companies show "prior and extensive use" of a product in order to be approved for the protection, the source

says. Many biotech companies are young and research-oriented, and are working on their first products.

The House-passed plan also would require that applicants have comprehensive liability coverage, which is almost impossible for many biotech companies to obtain.

President Bush issued an executive order October 2001, broadening another executive order signed by President Eisenhower in 1958. Eisenhower's order authorizes the Department of Defense (DOD), the armed services and several other cabinet-level agencies to shield defense contractors from liability. The order covers third-party claims for death, personal injury or damages to property and reasonable costs of litigation and settlement.

However, a BIO source says the broadened order still is too narrow and points out that DOD rarely has used it. Both the original and new executive order would only help shield from liability companies that contract with the government. The order allows indemnification only when risks are "unusually hazardous," and the currently held definition for this term likely would not cover the risks involved in producing biodefense drugs and biologics, industry sources say. Under the order, companies and the government must still outline the terms of the indemnification. If someone were to sue a company over a serious side effect caused by a vaccine or drug, the claim may not fall within the terms of a given contract, leaving companies open to lawsuits.

Another shortcoming in the 1958 executive order is that obligations in excess of $25 million cannot be entered into until Congress has been in continuous session for 60 days and after the congressional Armed Services Committees have been notified, according to the source.

FDA ASSERTS ITS AUTHORITY OVER 'PHARMERS' OF DRUG-PRODUCING CROPS

With the advent of a new form of biotech drugs, FDA is asserting its authority over growers of bioengineered pharmaceutical-producing plants with plans to treat such crops as manufacturing facilities. FDA's move is prompting debate over FDA's regulatory role, with a key consumer advocate group calling for even stricter FDA controls to ensure such plants are safe if they end up in the food supply.

The Center for Science in the Public Interest (CSPI) wants Congress to require FDA pre-market approval of all genetically engineered crops, including pharmaceutical plants, to ensure they are safe if they end up in the food supply.

Plant-made pharmaceuticals are therapeutic agents (pharmaceutical proteins) that biotech companies produce in plants. Crops such as corn, tobacco, rice and soy are genetically altered to yield proteins that are equivalent in purity and activity to those produced by other manufacturing systems. These bioengineered crops differ from edible vaccines, which are plants that vaccinate those who eat them.

Speaking at a Pew-sponsored biotech food conference last month, Keith Webber of FDA's biologic center said all aspects of "pharming" — including seed banking, prepping the field, planting, cultivating, harvesting, storage, extraction, and purification of the final product — are subject to the same good manufacturing practices (GMPs) as traditionally produced biologics.

FDA also plans to inspect these farms as a condition of approval for a drug that uses a protein extracted from such plants, Webber said, and the agency will inspect the farms postmarket. These inspections entail evaluations of the farm, as well as audits of records and data.

Bradly Shurdut of Dow AgroSciences said plant-made pharmaceuticals always will be highly regulated, unlike commodity biotechnology products, which are deregulated after going through an extensive risk assessment process prior to commercialization. Shurdut added that the U.S. Department of Agriculture ensures that the crops are confined so that they do not contaminate the food supply.

However, Gregory Jaffe of CSPI said inevitably these drug-plants will get into the food supply, and complained that no agency is responsible for ensuring that these crops are safe to eat.

FDA has a voluntary notification process for some genetically engineered crops, but that process does not capture pharmaceutical plants, Jaffe said, consequently those plants receive no FDA food-safety assessment. He recommended that Congress establish a mandatory pre-market approval process at FDA for all genetically engineered crops, including pharmaceutical plants.

Drug-producing crops promise to be a huge industry, according to a spokesperson for the Biotechnology Industry Organization (BIO). Industry representatives say there are about 80 to 100 drugs being developed from plants for monoclonal antibodies, the spokesperson says, and industry hopes that by 2010 about 10 of these will be going through the approval process. Currently proteins primarily are extracted from animals, but plants are cheaper, more prolific, and there is no threat of transmitting viruses or mad-cow disease, the source says.

Farmers are specially trained and certified by the feed manufacturers that contract with them, the spokesperson says. They grow the plants in small numbered plots, usually 10 to 20 acres. USDA is in charge of ensuring that farmers wait the appropriate length of time until after nearby commodity crops have been planted, along with other rules such as keeping the plants all male or making sure corn is detassled. However, each crop is unique, and USDA will treat each one differently accordingly, the spokesperson says.