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Consumer Health Focus

FDA's OTC Naloxone Study Is A Starting Point For Other Switches, Not A Roadmap

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An FDA study on expanding access to opioid overdose-reversal medication could suggest a model for Rx-to-OTC switch proposals that include some form of extra-label information, though the agency isn't going so far as saying the results will facilitate approvals for more nonprescription ingredients.

FDA Center for Drug Evaluation and Research officials said during an industry conference on May 11-12 that the agency for one year has been developing and testing labeling that instructs consumers on administering the opioid receptor antagonist naloxone through intramuscular injection or nasal delivery to a person experiencing an overdose. The study labeling includes pictograms separate from Drug Facts label (DFL) text.

"We've actually put money behind this to test this in a label comprehension study," said Division of Nonprescription Drug Products Director Teresa Michele during a panel discussion on FDA's OTC drug programs on the second day of the Consumer Healthcare Product Association's Regulatory, Science and Quality Conference in Bethesda, Md.

Pharma firms, meanwhile, often look askance at putting money behind research for novel OTC switches needed to develop some form of extra-label information, such as instructions or questions accessed online, to facilitate safe OTC use of a drug. Although FDA encourages firms to ask CDER about potential novel switch proposals for chronic conditions, such as high cholesterol, diabetes and hypertension, the agency currently does not have enough answers on criteria for success to assuage manufacturers' doubts about spending even to prepare information for a pre-new drug application meeting.

Teresa Michele, director of CDER's OTC drugs division

CDER Director Janet Woodcock

Michele said the naloxone study could spur industry interest in resolving an unmet public health need by conducting tests and preparing an application for a product that would face a difficult evaluation for approval. CDER would require a potential naloxone switch sponsor to conduct its own testing as part of its application.

"We recognize that there's a barrier to switch and it's a big obstacle to some companies. We said, 'What if we took the first step and started that development process ourselves,' so we could provide that information to companies who might be considering a switch," she said.

"If there are any manufacturers who might consider this, please come talk to us," she added.

Pfizer Inc. took a swing at preparing a new drug application for a 10 mg version of its blockbuster high cholesterol drug *Lipitor* (atorvastatin) with a 1,200-subject actual use trial completed in December 2014. It halted the program and did not file an NDA after the trial did not meet its primary objectives of demonstrating patient compliance with the direction to check their low-density lipoprotein cholesterol level and, after checking, to take appropriate action based on test results. *(Also see "Light Still On For Switches After Pfizer Pulls Plug On OTC Lipitor" - Pink Sheet, 3 Aug, 2015.)*

Pfizer has not turned away from considering OTC switches for chronic conditions, though. The firm could be preparing a proposal for an OTC *Viagra* (sildenafil) indicated for erectile dysfunction, an indication **Sanofi** is targeting with its own program to develop a switch application for *Cialis* (tdalafil) on license from innovator **Eli Lilly & Co.**

PICTOGRAMS SEPARATE FROM DFL

Labels for OTC drugs, other than those intended for pediatric use with administration by an adult, typically state indications and dosing directions for the person using the product. In contrast, directions on nonprescription naloxone products would instruct a person on how to administer it to a second person. That would be similar to instructions for aphylactic shock remedies.

Those directions would include advice on signs that a person known or suspected of abusing opioid- or opiate-containing drugs

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could be in danger of overdosing as well as on administering the treatment.

Naloxone most commonly is administered by emergency medical personnel and by medical staff in hospitals. Several firms have approvals for intramuscular injection products. **Adapt Pharma Ltd.** has approval for a nasal delivery formulation, *Narcan* Nasal Spray, and several other firms previously had approvals only for intramuscular injection products. *(Also see "Bring Naloxone To Opioid Overdoses: FDA Crowd-Sources Smartphone Apps" - Pink Sheet, .)*

"Obviously, there are rarely health care personnel around when overdoses occur in various settings. So we need something that is broadly available that people can use quickly," said CDER Director Janet Woodcock in her conference-opening presentation.

Pictograms CDER is testing on labels show "how to safely use naloxone, including when it's appropriate to purchase it and how to use it in an emergency opioid-overdose situation," Woodcock said.

The ongoing consumer label comprehension study will provide information potentially helpful to firms interested in proposing other OTC switches. The agency will publish the study results regardless of whether the testing shows that consumers correctly self-select and use the product through the instructions and other information on the labeling.

"If it's successful then the industry can adapt it to their product," Michele said, but added that in the event the test results are not a success, "I think the labeling still will be valuable."

FDA started the work "in the face of this epidemic of deaths due to opioid overdoses" caused by either pharmaceuticals or illegal narcotics, Woodcock said. "We are very interested in getting this program complete and getting this information out there and hopefully attracting manufacturers into this space," she added.

NO ANSWERS YET FROM NSURE

Any ideas emerging from the naloxone study might be particularly helpful given that industry is still waiting for more guidance to come out of the Nonprescription Safe Use Regulatory Expansion initiative CDER launched in 2012.

SMARTPHONE APPS APPROPRIATE FOR OTC PRODUCT INSTRUCTIONS – CONSULTANT

FDA and the industry should get up to speed on incorporating smartphone apps to provide instructions on OTC drugs, says Saul Shiffman, senior scientific advisor for behavioral science, study design and analysis at pharma industry consultancy Pinney Associates.

Consumers' rampant and still increasing use of mobile apps for all manner of lifestyle, commerce and communications functions demonstrate that the time has come for linking OTC labels with digital tools, said Shiffman, a professor in the departments of psychology and pharmaceutical science at the University of Pittsburgh, on May 11.

"The use of appropriate technology could enable us to do much more than we do with the DFL," he said, adding, "We're not only not in the future, the present has passed us by."

Shiffman spoke at the Consumer Healthcare Product Association's Regulatory, Science and Quality Conference in Bethesda, Md. Key topics at the meeting included how to communicate information outside of an OTC product's label, such as through instructions accessed online, to support safe use (*see sidebar*). Such information is needed as part of novel Rx-to-OTC switches.

To modernize FDA's oversight of OTC labeling, Shiffman suggested creating "a trial of breadcrumbs to help the regulatory thinking to go from the current thinking that the DFL [Drug Facts label] is everything to allowing the app to have a role and eventually to supplant the DFL."

"At some point I could imagine a label that said what the indication is, you have to know what you're treating, and then the label would say use the app and give you a link," he said.

Although entirely digital Drug Facts labels are far from even being considered as a potential step, Shiffman added, FDA and drug marketers should be concerned about providing some information on a product's DFL and referring consumers to an app for the remainder.

"I think there's actually some risk potentially in trying to have some stuff on the Drug Facts label and some stuff on the app lest consumers think the drug facts label is complete and not go to the app."

Nonetheless, guiding consumers to accurate self-selection of an OTC drug indicated for a chronic condition is unlikely using only a printed DFL, Shiffman.

"The easy switches are behind us," he commented, adding, "Apps become more potentially more important as a way to overcome some of those hurdles."

Under NSURE, the center continues looking into potential changes in its switch application process so sponsors could propose novel switches, including ways to expand communications on safe use beyond the DFL. *(Also see "Room For Innovative Switches Could Lurk In Existing FDA Framework" - Pink Sheet, 29 Oct, 2014.)* "While there hasn't been anything out on that yet, we have been exploring internally on how to make that happen and what may be required," Michele said.

At the 2016 CHPA regulatory conference, a CDER attorney said the center was working on a framework for implementing changes, most likely requiring a rulemaking by FDA, that would allow the agency to base approval of an OTC new drug application partly on information not within a Drug Facts panel. *(Also see "CDER Talks Switches, Monograph 'More Than Ever,' But Mum On Changes" - Pink Sheet, 23 May, 2016.)*

However, neither CDER official offered an update on when FDA might propose NSURE-derived changes for the OTC switch process. "You the industry have been asking us about this for a long time," Woodcock acknowledged.

"There could be potential for restricted-access programs to aid in self-selection and other safe use areas, ways to put some guard rails in to make sure the right people are taking these medicines or directing them to a health care provider if that's what's needed," she said.

FDA realizes that without guidelines adopted in a rulemaking, pharma firms need communication directly from CDER officials on preparing a novel switch NDA.

"Because these programs do raise novel legal, regulatory and scientific considerations, we are encouraging sponsors to come in and talk on a product-by-product basis to the division while we're working out the framework for putting in those guard rails," Woodcock said.

NOVEL SWITCHES, COMPLICATED PATH

FDA was encouraging firms making Rx drugs indicated for chronic conditions to ask about potentially submitting applications to make additional ingredients available OTC before making its interest official with NSURE. *(Also see "The Future Of OTCs: Self-Selection Meets Diagnostics, Genetic Personalization" - Pink Sheet, 16 May, 2011.)*

However, agency officials have not indicated they have a solution for the conundrum drug firms eyeing OTC switch proposals must consider: when a drug is available on store shelves, health care providers aren't there to advise consumers on whether they need to use it or train them on administering it.

OTC drugs generally are indicated for symptoms easily apparent, such as a headache or cough/cold, and a product's efficacy is just as easily determined. But chronic conditions that FDA would like targeted by some OTCs are not so easily apparent and a product's treatment efficacy is a more complicated question to answer.

Novel approaches for OTC status could include the use of technology or label restrictions to help consumers correctly self-select and safely use under "conditions of safe use." Some health care groups and consumer health advocates support making pharmacists' counseling with consumers a component of novel switches, but FDA's regulatory oversight does not extend to pharmacists' responsibilities and agency officials have dismissed imposing those requirements.

Still, drug firms are aware FDA will not answer the questions Woodcock noted as inherent in novel switch applications, and thus are discouraged from investing in preparing an idea to pitch in a meeting with CDER.

Moreover, current FDA regulations prompt other investment concerns for potential sponsors of novel switch proposals: the agency could not subject eventual generic versions to the same extra-label requirements that the agency might have made for the innovator's switch, and unless a clinical trial is required for a switch NDA, the sponsor would not be eligible for any period of market exclusivity for its product. *(Also see "FDA To Tackle Critical Generics Issue In Switch Paradigm Debate" - Pink Sheet, 12 Mar, 2012.)*

Two-Tier OTC Monograph Approach Could Come With User Fee Revamp

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Industry could have two tracks for seeking changes to OTC products marketed under the US monograph system: one for adding new ingredients or medical conditions treated by those ingredients, which would be eligible for exclusivity when clinical trials are required, and another for other types of changes.

The approach is proposed in a discussion draft of legislation to create a user fee program for OTC products, authored by Sens. Johnny Isakson, R-GA, and Bob Casey, D-PA. The new approach, intended to encourage adding new ingredients to monographs and speeding FDA reviews, would be the return on investment for paying user fees, which could total up to $34m per year. *(Also see "OTC Monograph User Fees Totaling $22m To $34m Floated In Senate Discussion Draft" - Pink Sheet, 19 May, 2017.)*

The plan would be added to pending legislation to reauthorize existing drug and medical device user fee programs, and, like those programs, reflects FDA/industry agreement.

Similar to the Sunscreen Innovation Act Congress passed in 2015 to encourage adding new ingredients to the OTC sunscreen monograph, the discussion draft Sens. Isakson and Casey circulated May 10 proposes deadlines for FDA reviews for the other monograph categories.

Monograph proposals, under the senators' draft, would become "requests" and firms or other parties submitting them would be "requestors," rather than sponsors, as FDA uses to identify the sources of new drug application proposals.

Monograph requests would be categorized as tier 1, which would develop monographs for new ingredients or add new medical conditions to existing monographs, and

tier 2, which would be for making changes to approvals for existing ingredients, such as updates to safety updates to product labeling.

FDA would have authority to request human clinical trials for tier 1 requests. If it does, the manufacturer would be eligible for up to two-years market exclusivity. This resembles a component of the agency's rule for Rx-to-OTC switch applications that allows three years of exclusivity for proposals that must include clinical trial data.

"That would mean that once the conditions are changed the requestor would have exclusive rights to those new conditions for a period of time," said Greg Collier, regulatory and safety director for **Procter & Gamble Co.**, said in a presentation at a recent Consumer Healthcare Products Association conference.

The tier 2 category is not yet defined as clearly as tier 1, though requestors will pay fees for both types. "We're going to actually grow into this as an industry and so will FDA. But when we start those tier 2 innovations will be clearly spelled out and everything else will be tier 1 innovations," Collier said.

According to the discussion draft, the user fees for requests will be $500,000 for tier 1 and $100,00 for tier 2. Fees will be waived for requests to change labeling to improve safe use of an ingredient, and different amounts of the fees will be refunded when a requestor withdraws an "OTC monograph order request" (OMOR) and when a request is re-classified from tier 1 to 2.

PROGRESS BY THE DASHBOARD LIGHT

Targeting the lack of transparency in the current monograph system, the proposal agreed to by the agency and the industry includes a requirement that FDA at least once annually post an online "dashboard" about its monograph plans.

Barbara Kochanowski, CHPA's regulatory and scientific affairs chief, anticipates that industry stakeholders might be underwhelmed by an FDA exercise in publishing its goals. The monograph dashboard, though, won't be a narrowly targeted unified agenda by another name.

"We don't envision this to be a unified agenda type dashboard that we all look at and go, 'OK maybe.' This is really going to be FDA's best estimate of priorities on when they intend to attack different ingredients," Kochanowski said.

FDA would have to conclude reviews in less than two years, under the proposal. The clock would start with FDA having two months to decide whether a request will be reviewed or needs additional information. The agency would have 10 months to decide whether to approve or deny tier 1 requests and eight months for tier 2 submissions, followed by a 45-day comment period, two more months to assess the comments and another eight weeks to draft an order.

Collier also described a third option for submitting OMORs for marketing a product a different dosage device than currently allowed by a monograph. FDA would have to publish an order and guidance to define the third option fully as "kind of a middle ground of innovation that will be available," he said.

Additionally, as they are with investigational new drug proposals and NDAs, firms are encouraged to meet with Center for Drug Evaluation and Research staff at least 120 days before making OMORs.

"More or less like a pre-IND or a pre-NDA meeting where you can talk real specifics about what's going into the request," Collier said.

While this new approach is intended to address industry calls for monograph program reform, the bulk of the user fee funds are expected to come from facility registration fees rather than tier 1 and 2 OMORs.

OTC Monograph User Fees Totaling $22m To $34m Floated In Senate Discussion Draft

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A proposal to raise $22m to $34m in annual user fees from OTC manufacturers – primarily from facility registrations – is contained in a discussion document being circulated by Sens. Johnny Isakson, R-GA, and Bob Casey, D-PA.

Fees would also be raised when companies request changes via the monograph system, which would be recast into a two-tier program. *(Also see "Two-Tier OTC Monograph Approach Could Come With User Fee Revamp" - Pink Sheet, 19 May, 2017.)*

While the current proposal does not detail how much would be raised from registering manufacturing facilities with FDA versus requesting monograph changes, the majority of the funds are anticipated to come from the former. Some industry leaders, including the Consumer Healthcare Products Association, view facility fees as spreading the financial responsibility more broadly and creating a more predictable funding source than monograph requests.

In return, industry would see changes to streamline the monograph system, which governs when ingredients are recognized

as safe and effective for the US OTC market and which medical conditions those ingredients can be claimed to address. The system has gotten so bogged down and cumbersome that FDA drug center chief Janet Woodcock called it "frozen in amber" at a recent OTC industry conference.

The possibility of new user fees to support monograph changes has been discussed for a least a couple years and the Isakson/Casey discussion draft contains provisions negotiated between FDA and OTC industry stakeholders, but the specific details have not previously been disclosed.

The proposal would move forward by being attached to legislation already moving through Congress to reauthorize FDA's existing user fee programs.

The Senate Health, Education, Labor and Pensions Committee passed and the House Energy and Commerce Health Subcommittee moved to full committee separate versions, S. 934 and H.R. 2430, of the FDA Reauthorization Act (FDARA). The must-pass legislation would continue for five years the agency's existing user fee programs for drugs and medical devices. The programs would no longer stand if Congress does not pass a reauthorization bill by Sept. 30, the end of the federal fiscal year. *(Also see "Breakthrough-Style Program For ANDAs Added To House User Fee Bill" - Pink Sheet, 18 May, 2017.)*

Time is limited, however, for adding an OTC component and completing work on the overall user fee package.

"The time window is short and we certainly hope that people take this seriously and it will be considered," Woodcock said in opening remarks to the Consumer Healthcare Products Association's Regulatory, Scientific and Quality conference May 11-12 in Rockville, Md.

"We've been negotiating and engaging with [industry] via ongoing monograph reform discussions for quite some time," she noted.

At the event, Barbara Kochanowski, CHPA's senior vice president, regulatory and scientific affairs, acknowledged that some on Capitol Hill say OTC monograph reform and user fee legislation has "missed the window" this year while others say the "window's still open."

"As long as there is a legislative champion there is a possibility this can happen," Kochanowski said.

> "Probably many folks at FDA and people who have been in the industry for many years may not even be aware of all the nuances in the OTC monograph." – FDA's Teresa Michele

Adding the changes to legislation reauthorizing FDA's existing user fee program likely will take a champion in a House and Senate conference committee to work out differences in the two chambers' bills.

Kurt Karst, a food and drug lawyer following FDARA discussions in Congress, noted that the OTC issues were not mentioned before the Senate HELP Committee and the House Health Subcommittee voted on the separate bills.

"That being said, if there's a conference committee, there may be an attempt to add it there. If not now, it could be five years … but I suspect that there would be an effort beforehand," said Karst, a director at Hyman, Phelps & McNamara P.C. in Washington.

RULEMAKING PROCESS STALLED MONOGRAPH CHANGES

FDA launched the monograph program, following congressional authorization, in 1972 as a system for allowing OTC ingredients generally recognized as safe and effective for their intended uses to remain available and for offering drug firms and other parties a process for proposing additions of more ingredients or indications. *(Also see ""No End In Sight" For Completing OTC Monographs – CDER Director Woodcock" - Pink Sheet, 26 Mar, 2014.)*

The monograph includes essentially a menu of ingredients and formulations that can be used in drugs for certain indications, and what has become a byzantine maze of rulemaking that must be navigated for any addition to change, no matter how small or how urgently needed, to any part of the monograph. In contrast, of course, FDA need not go through formal rulemaking to approve new prescription drugs.

The monograph program has been stalled for much of its 45 years and FDA and industry stakeholders identified reforming the program as a nonprescription sector priority well before they began negotiations on a proposal in June 2016.

"The pace of completing the monograph system has really come almost to a halt," Woodcock said at the CHPA event. "There's no innovation really possible in an area that would be a significant innovation. We really have challenges in safety, because of our inability to respond quickly when safety problems arise."

When the monograph system launched, rulemakings for all federal agencies could be completed much sooner. However, the introduction of notice-and-comment periods and of Office of Management and Budget reviews added layers of complexity and years to the timeline in proposed rulemakings.

With rulemaking "the heart and soul of" the monograph process, the time has passed when "things just moved along," Kochanowski said. "We haven't seen that in a long, long time."

Moving the monograph system from a rulemaking to administrative process, conducted within FDA without review by OMB, should produce a final decision within two years of a proposal's filing with the agency.

"Even much faster in the case of safety issues or where there's a need for very quick changes," Kochanowski said.

REFORM COMES AT A COST FOR ALL

FDA opened a docket for comments on monograph reform two years before a separate docket about user fees to pay for its work, and it's been clear since that the monograph program would not improve without additional funding. *(Also see "All Roads For OTC Policy Improvements Lead To User Fees, FDA Suggests" - Pink Sheet, 7 Sep, 2016.)*

"It would be very nice if this all came for free," Kochanowski said, adding, "FDA would probably like even more money than we've come to an agreement on and industry would like to pay less."

While some in the industry supported basing user fees only on monograph proposals, fees linked to manufacturing facility registration also are needed to assure that all firms making products approved

through monograph additions or changes will bear some of the program's costs.

"Our objective is to spread the payload as widely as possible, as broadly as possible, so that everyone with a stake in OTC monograph products is contributing. We have no doubt that this will continue to be discussed going forward," Kochanowski said.

Additionally, annual facility registration fees can be calculated in advance. "We need to offer a predictable resource of revenue and that is the thinking behind the facility fee model," she said.

The FDA and industry agreement detailed in the discussion draft calls for monograph drug firms to pay totals of $22m to $34m annually over the five-year authorization of the program and for FDA's direct appropriation for all of CDER's OTC programs to grow from $8m to $12m during that period.

"We could find that we asked a lot more of FDA than we agreed to pay for and we could find that we need other things that we haven't talked about," Kochanowski said.

In addition to determining whether the monograph user fee totals are sufficient, FDA will measure the effectiveness of the program on its success in adding staff infrastructure needed to add to support the work as well as on the number of additions or changes made to the monograph.

Teresa Michele, director of CDER's Office of Nonprescription Drug Products, explained that two years are needed for training staff in the office's programs and policies. "Probably many folks at FDA and people who have been in the industry for many years may not even be aware of all the nuances in the OTC monograph," Michele said.

FDA would be required to provide guidance on multiple components of the changes and an annual letter to industry stating its goals for the program.

The infrastructure changes would include adding a section on monograph requests to FDA's website and converting the rules it has published for monographs into administrative orders. "Creating a new world and a new language for all of us to talk about," Kochanowski said.

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Navigating Amazon: E-Commerce Giant Critical For OTC Drug Sales

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OTC drug and other consumer health product firms that are avoiding Amazon as a sales platform put their businesses at risk if they continue ignoring its emergence as the dominant search engine for consumers.

"Amazon is a search engine, it is the number one source for product research," said Lynn Graham, founder and president of BeeKeeper Marketing LLC, which develops strategy for consumer packaged goods marketers who sell products on Amazon.

"Fifty-five percent of consumers don't go to Google to research products, they go to Amazon," she said recently at the Consumer Products Association Annual Executive Conference in Amelia Island, Fla.

"Even if you are not ready to go on right now – say you don't have the right package sizes – and even if you think you're not going to sell a lot on Amazon right now, it still makes a lot of sense from a marketing perspective to be up there on those pages," said Graham.

She noted data from a 2,000-person survey conducted by BloomResearch, which helps e-commerce firms personalize their sites' buying experience, showed that 28% of consumers use the big search engines Google, Bing and Yahoo and 16% look to retailer websites *(see graph, p. 8)*.

The data demonstrate a sizable leap for Amazon over the prior year, when 44% of consumers said they turned first to Amazon for product information, 34% sought information on other search engines and 21% turned to retailer websites, according to BloomResearch.

Additionally, sales for the health and wellness sector of Amazon demonstrate conversion rates – moving from search to purchase – are also strong on the site. Amazon's total health and personal care sales in 2016 reached $4.7bn, up 35% from 2015, according to e-commerce research firm One Click Retail. One Click noted in a March 23 report that total sales in the US health and personal care market – both online and in stores – was $336bn in 2016.

One Click also pointed out that Amazon's health and personal care sector, including OTC drugs, dietary supplements, non-drug topicals and at-home medical devices, is growing close to five times faster than the total US sector. Significant year-over-year increases were shown in nutrition and wellness, 40%, health care, 45% and beauty, 47%, according to the researcher.

OTC products, sub-categorized as "health care" among consumer products in One Click's survey, grew 45% on Amazon year-over-year in 2016.

Despite the growth, though, health care sales on Amazon face competition from retail stores, as many consumers prefer to buy OTC drug products in brick-and-mortar. "The reason for this is either because of urgency (many of these items are only bought as they are needed), or because they're viewed as more 'sensitive" items that some people may be less comfortable with ordering online," One Click researchers said.

Amazon lists "best sellers" for each OTC drug category on its site, updated hourly *(see chart, p. 8)*.

LOOKING FOR 'BUY BOX' STATUS

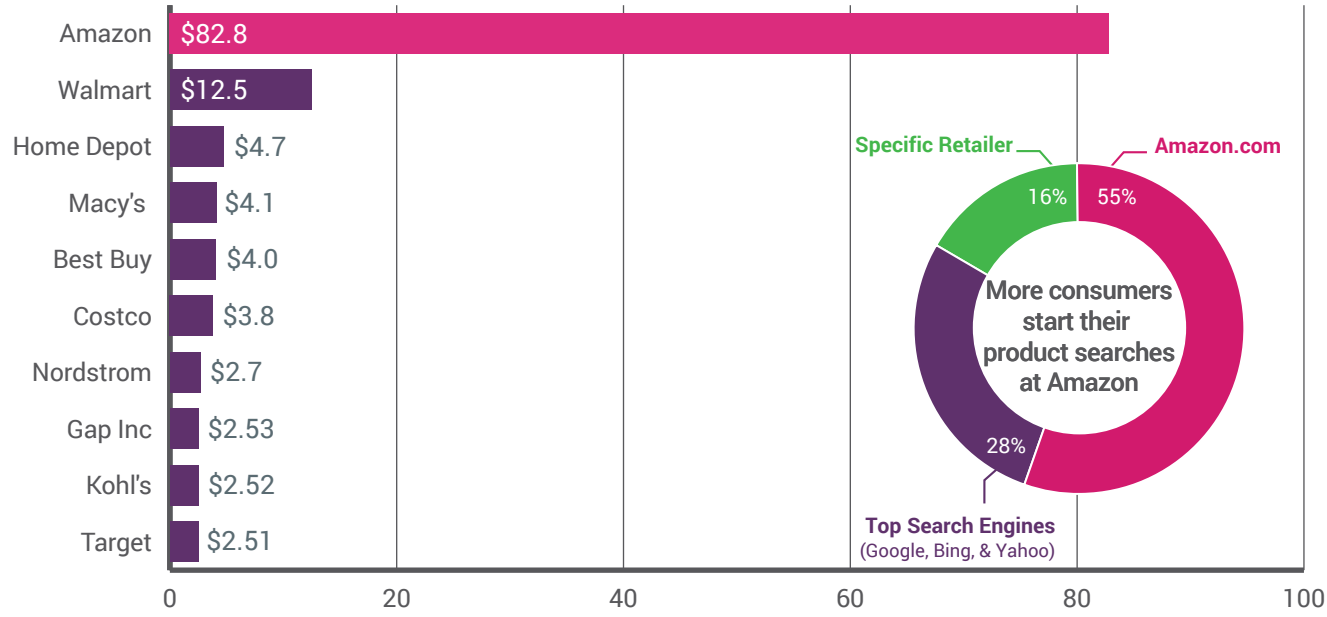
"Everyone knows e-commerce is here to stay. And Amazon is of course the biggest in the space, so before you even think about the number two players, given the size of Amazon, you need to make sure you are getting it right with them first," Graham said.

Amazon allows vendors to operate as either direct selling and third-party accounts, Graham noted. Direct sellers offer products on the Amazon Vendor Central interface, where vendors are considered first-party sellers. These companies act as suppliers, selling directly to Amazon, and their products are displayed on the site with the phrase "ships from and sold by Amazon.com."

In determining direct-seller vendors' product prices, "Amazon has an algorithm

INDICATION	AMAZON'S TOP 3 SELLERS BY OTC CATEGORYON APRIL 24, 2017, NOON EDT / MANUFACTURER
Allergy Relief	*GoodSense All Day* Allergy (cetirizine); **Perrigo Co. PLC**
	Zyrtec Allergy (cetirizine); **Johnson & Johnson Consumer Inc.**
	Flonase Allergy Relief (fluticasone); **GlaxoSmithKline Consumer Healthcare LP**
Sinus Relief	Allegra 24Hr Adult (fexofenadine); **Sanofi**
	NeilMed Sinus Rinse Refill Packets (saline); **NeilMed Pharmaceuticals Inc.**
	Claritin Children's Chewables (loratadine); **Bayer HealthCare LLC**
Cough & Cold	*Infants' Tylenol* Oral Suspension (acetaminophen); **J&J Consumer**
	Boiron Oscillococcinum for Flu Symptoms (homeopathic); **Boiron USA**
	Xlear Xylitol Sinus Care Spray (xylitol and saline); **Xlear Inc.**
Antacids	GoodSense Omeprazole Acid Reducer; **Perrigo**
	Nexium 24Hr (esomeprazole); **Pfizer Inc.**
	Prilosec OTC (omeprazole); **Procter & Gamble Co.**
Aspirin	*Bayer* Aspirin; **Bayer HealthCare**
	Kirkland Signature Low Dose Aspirin 81mg (single- and two-bottle packages); **CostCo Wholesale Corp.** store brand also available at other retailers

Amazon Dominates Shoppers' Bandwidth*



(sales in billions) Amazon is the leading e-commerce site for consumer packaged goods with sales for the past 12 months more than six times greater than No. 2 Walmart, and it's securing its position as the online destination for consumers' product searches.*

Source: Beekeeper Marketing research

that looks out into the marketplace and their strategy is, they want to be fair relative to brick and mortar, but they want to match the best price for other online competition," said Graham.

To be eligible to earn Amazon's recommendations among similar products, which it labels "buy box," a vendor must meet certain standards on shipping proficiency, inventory status and positive reviews; when multiple sellers meet those standards, Amazon gives a "buy box" to the lowest priced option.

Third-party vendors list items on Amazon Seller Central, the interface merchants use to manage orders. Amazon's pay-as-you go system allows vendors to participate in "Fulfillment by Amazon," which manages shipping, customer service and returns.

However, third-party vendors often have a more challenging time winning a buy box because Amazon often considers direct sellers to have better metrics and its algorithms that determine buy box selections favor direct sellers.

Third-party sellers control the price of their products and often are undercut by competitors and lose the coveted buy box. Products in this area are labeled "Sold by [vendor] and fulfilled by Amazon."

"Launch as a direct vendor and as a third party for maximum sales opportunity and risk mitigation," but if a firm must choose, direct selling is better long-term, Graham said. "Your listing content will trump other listings, because you will always win the buy box as long as you are profitable" for Amazon.

COMPLIANCE PAYS OFF

Graham trains her clients' operations and supply chain managers on Amazon's expectations for turnaround time, labeling and other issues. "Because it is labor intensive, and there are some [firms] that just won't do it, or they'll do it and not do a good job" and have to pay for charge-backs, or refunds to the customers, she said.

"I see businesses that do amazing on the sales and marketing side, that end up shutting down because they are hemorrhaging so much in terms of charge backs for noncompliance" with Amazon's policies.

"Really build with e-commerce in mind, not as an afterthought, especially when it comes to pack sizes," Graham said. "One mistake I see a lot of folks make is they optimize for brick and mortar and then they consider [e-commerce] as an afterthought. It's a lot easier to do the right thing when you think about it up front."

Amazon either sells products "by the each" – or per product – or by the case. "The default is that they are going to sell it by the each as long it's profitable, otherwise, they will see it by the case and they will only sell it by the case of they think the consumer will buy it by the case."

She recommended at least $10 for an individually sold product price so Amazon can find a profit margin. "If you are a company with a product that is at a price point of under $10, Amazon is now going to set it up by the case, and then you are going to have to think to yourself, 'is the consumer actually going to buy this by the case?'"

During her presentation, Graham was asked whether Amazon responds when a competitor or a consumer places untrue, disparaging information in the comment section of a product's sales page.

If untrue, negative statements about a high-selling product are posted the seller's site, "you can usually get the attention of your Amazon vendor manager and they can help" resolve the issue, she said.

On the other hand, Amazon founder and CEO Jeff Bezos "is clear that customer comes first on everything. If it's a food safety or legal issue and Amazon lawyers typically respond proactively in the case and are quick to shut down sales," Graham said.

Amazon limits communicating with consumers and vendors should promote products or educate consumers about items off the site, too.

"If you have a really cutting-edge, new product that requires a ton of education, more than you can explain in a quick search advertisement, you really need to be thinking about what you can be doing outside of Amazon to educate consumers. I think that can be the challenge. Amazon is a hard place to educate people," Graham said.

Codeine Concerns Cough Up FDA's OTC Monograph Problems

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FDA recently ordered label changes for Rx codeine drugs but could do nothing immediately and directly to affect marketing of OTC monograph drugs containing the ingredient. This disconnect provides more evidence that FDA should be empowered with flexibility to address these kinds of situations, as it can for prescription drugs, consumer health industry stakeholders say.

Additionally, the Pew Charitable Trusts suggests the case is clearly made for establishing user fees to support FDA's work in determining whether drug ingredients are safe and effective for a monograph indication by the big difference between funding for FDA's Rx drug evaluations and the monograph program.

Pew joined the Consumer Healthcare Products Association and medical groups recently in urging the Senate Health, Education, Labor and Pensions Committee to create a user fee program to support OTC monograph work and transition the monograph system from formal rulemaking to a more flexible administrative process. They advocate that these changes be included as part of legislation to reauthorize user fees for prescription drugs, biosimilars and generic drugs.

"FDA really needs the resources to be able to do this right now," said Kirsten Moore, PEW's health care products project director.

FDA's evaluation and ongoing oversight of OTC drugs made available after pre-market approval through new drug applications (NDAs) is supported in part by user fees. However, the large majority of OTC drugs available in the US are marketed under the monograph system, which acknowledges ingredients and formulations as generally regarded as safe and effective for certain indications and which FDA currently manages strictly through appropriated funding.

Moore pointed out that while annual OTC sales in the US are estimated at $32b and the market comprises some 300,000 prod-

ucts, FDA staffing assigned to monograph work is fewer than 30 full-time equivalents.

"They're outmatched right now," Moore said in an interview.

Meanwhile, codeine-containing OTCs are still on the market despite FDA's April 20 order for Rx product labeling changes to reduce the pediatric risk of life-threatening respiratory depression with codeine.

In their April 28 letter to Senate HELP leadership, Pew, CHPA and their partner groups urged that Congress "adopt comprehensive monograph reform."

"Under the current regulatory process, publishing a new or amended OTC monograph requires the FDA to go through a formal rulemaking process, which may take years, or even decades, to formally resolve. Until the FDA finalizes pending changes on a monograph, OTC products with unsafe or ineffective ingredients can legally remain on the market," the letter states.

FDA ON OTC CODEINE: READ THE LABEL

Douglas Throckmorton, deputy director of regulatory programs in FDA's Center for Drug Evaluation and Research, said during an April 20 media briefing on the Rx product label changes that the agency's action on OTC products was limited to advising consumers to read product labels. *(Also see "Opioids: FDA Eyes Better Prescriber Education, But Academics Urge Promotion Crackdown" - Pink Sheet, 20 Apr, 2017.)*

"Because many cough and cold products are available over the counter, the FDA also encourages parents to review the ingredients of those medicines and consult their health care provider before giving their children any medicines containing codeine," Throckmorton said.

He acknowledged the separation between the agency's Rx and NDA OTC drugs oversight and its monograph product system. According to a transcript of the briefing, he said "the regulation of over the counter products and prescription products is slightly different."

"We're in the process of reviewing … what needs to be done in the over-the-counter area. And … as soon as we have made a decision, obviously, we'd announce anything that we could," he added.

Pew doesn't expect FDA to act soon on potential label changes for OTC monograph codeine products about use by children 12 and under, or by women who are pregnant or nursing.

> FDA's "regulation of over the counter products and prescription products is slightly different."
> – Douglas Throckmorton, CDER deputy director of regulatory programs

"FDA does not have authority under the current rubric to take swift action, other than extending their recommendation in the prescription drug space to the over-the-counter space, which is just kind of counter-intuitive," Moore said.

"They have to go through this rulemaking procedure in order to actually change the [labeling] requirements for manufacturers. They've looked at the science and they have definitely concluded, and an outside advisory committee has strongly agreed that this is a potentially dangerous ingredient. But they are kind of hamstrung by the rulemaking process to come to a quick conclusion."

FDA is contraindicating the use of codeine to treat cough or pain and, as part of the same announcement, the use of a second type of opioid drug, tramadol, to treat pain, in children younger than 12. It also is adding a warning to the labeling of codeine and tramadol products recommending against use in adolescents between 12 and 18 who are obese or have conditions such as obstructive sleep apnea or severe lung disease that may increase the risk of serious breathing problems.

Tramadol labeling also will add a contraindication against use in children younger than 18 to treat pain following surgery to remove tonsils or adenoids. In 2013, FDA added a boxed warning to codeine labeling recommending against use in children following tonsil or adenoid removal surgery.

The codeine-specific recommendations do not go as far as urged by an advisory committee in December 2015, when the majority of the external experts recommended contraindicating for pain and cough in children younger than 18.

A majority of those experts also recommended removing from the OTC monograph for cold, cough, allergy, bronchodilator and anti-asthmatic products an indication of codeine in children younger than 18.

Several of them also said "codeine should not be available at all [OTC] for any age range and suggested removing it completely from the monograph due to risks of respiratory depression, addiction, opioid abuse, misuse, potential for diversion, variable efficacy, and concerns that consumers may not recognize risk factors for adverse outcomes," according to FDA's report on the meeting.

Although codeine is included in the OTC monograph for cough and cold symptoms in formulations also containing other medications, no products containing the ingredient are available directly to consumers on store shelves. Concerns about abuse of unintentional misuse of products containing the ingredient have steered firms away from marketing nonprescription codeine products directly to consumers.

However, FDA reported to the advisory panel that 28 states and Washington, DC, permit nonprescription sales of codeine products by pharmacies. Because the Drug Enforcement Administration schedules some cough syrup with codeine as a Class V controlled substance, states have discretion to allow nonprescription sales, though maintaining records of the sales and purchasers' identities is required.

States allowing nonprescription sales differ on maximum allowable quantities that can be purchased at one time, 60 mL to 240 mL; the amount of time required between purchases, 48 hours to 96 hours; and minimum age of a purchaser, 18 years to 21, according to FDA's briefing document for the advisory committee meeting.

SAME SYSTEM SINCE 1974

Congress established the monograph system to allow nonprescription ingredients believed, based on decades of use in the US, to be safe and remain available and to determine whether additional ingredients should be considered GRASE for certain indications and added to a monograph.

In their letter to HELP Committee lead-

ership, Pew and its colleague groups note the monograph system "was established in 1974 and has not been updated since."

Requiring a rulemaking for any addition or change in a monograph might have been considered appropriate at the launch of the system, but nearly 45 years later FDA officials and industry stakeholders alike agree the system is essentially gridlocked. *(Also see "New Home For OTC Drug Review Would Restore Momentum – Hutt, Yingling" - Pink Sheet, 27 Mar, 2014.)*

"It's a process whereby FDA oversees this giant marketplace through a rulemaking process, which is incredibly time-consuming and often is one step forward and two steps back," Moore said.

Moreover, as all federal agency rulemakings requiring review by White House's Office of Management and Budget, "you're bringing it into more of a political" rather than scientific process, she said.

FDA administrative authority, on the other hand, allows it to more efficiently and effectively evaluate and regulate Rx drugs and OTCs available through the application process. The agency's approval of those products makes them subject to label or formulation changes that may become necessary for safety or other reasons.

"The way that we review drugs, internally, science- and evidence-based, that is the same system we want to use for OTC products," Moore said.

And just as an application-based system for regulating other drugs shows what would work for monograph products, existing FDA user fee programs show the potential for garnering the agency additional support for its monograph work.

"This is a model that has worked for other components of the drug and medical device industries and that Congress has supported," Moore said.

"In addition to streamlining the decision-making process FDA needs resources to do their reviews and approvals. The user fee agreement that now exists for a whole variety of other categories of products is something we think is a good proposal for the OTC market as well," she added.

FDA in 2014 launched an initiative to improve and modernize the OTC monograph system, opening a docket for comments and conducting a public hearing for suggestions on improving the process. *(Also see "FDA Floats OTC Monograph Overhaul To Be "More Agile And Responsive"" - Pink Sheet, 24 Feb, 2014.)*

In a related but separate initiative, the agency in 2016 sought comments on asking Congress to authorize a monograph user fee program. *(Also see "OTC Monograph User Fees Inspire Wary Support From Industry" - Pink Sheet, 13 Jun, 2016.)* CDER and industry stakeholders conducted a series of meetings starting in August on agreeing on details of a proposal to submit to Congress. *(Also see "OTC Monograph Reform, User Fee Legislation Coming 'Any Day' – CHPA" - Pink Sheet, 30 Mar, 2017.)*

During negotiations on the details, CHPA said it expected a proposal would be part of legislation on reauthorizing FDA's existing user fee programs. *(Also see "OTC Monograph 'Disruption' Could Ride Along With PDUFA Reauthorization – CHPA Exec" - Pink Sheet, 22 Mar, 2016.)*

OTC Topicals Firm's Regulatory Problems More Than Skin Deep

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The marketer of *VenomX* and other topical OTC drugs would rather get out of the business than change following FDA's findings of good manufacturing practices problems and noncompliant claims including preventing diabetes-related amputations.

FDA's warning letter submitted on May 8 to **Phillips Co.**, owned by **Howard Phillips LLC**, of Sun City, Ariz., states that the company does not appear committed to correcting the GMP, labeling and branding problems Office of Regulatory Affairs officials found following in an October 2016 at its Millerton, Okla., facility.

The letter from ORA's Dallas District states in its response to inspectors form 483 findings, Phillips "acknowledged that your 'ability to build a pharmaceutical manufacturing company has been found lacking, as shown by the FDA inspection report.'"

Phillips' website largely confirms ORA's suspicions. A page in its product catalogue, which also offers information on the company's history and plans, states: "Intellectual Property for Sale. This is, in fact, the sale of Phillips Company." The statement is followed by a list of the treatment areas targeted by the firm's 20 OTC dermatology products and descriptions of its product development and the market potential linked to its intellectual property.

The sales pitch says company president and founder Howard Phillips is "known for his pioneering work in artificial vision, has developed 20 novel products for various skin conditions that have the potential to change, according to preliminary research, the treatment standards and standard of care" in diabetic wound healing; venomous snake and spider bite treatment; bacterial skin infections, including methicillin-resistant staphylococcus aureus; tissue regeneration via adult stem cell mediation; pain control; acne; and burns.

Shutterstock: Panchenko

The company also says its stem cell technology "is held as a body of trade secrets," but is not patented, though "the buyer of Phillips Company IP can seek patent protection if desired." Its product development plans stated in the catalogue include potentially renam-

ing its *TetraStem* product for periferal neuropathy and spinal cord injury indications.

Phillips says it focuses entirely on the development of topical products because it has "the world's most effective transdermal carrier technology," which is "a dual-carrier system that can carry any active ingredient through the skin and 2.5 cm into soft tissue with a therapeutically-adequate concentration of the active ingredient."

The sales pitch concludes by stating, "With the number of products, uses, market sectors and the sizes of the relevant markets, the possibilities cannot be overstated."

Phillips, however, is overstating the effectiveness of its *Tetracycline-ABC* and *Diabecline* brands as well as VenomX and TetraStem, ORA stated in the warning letter. Claims for the topicals render them unapproved new drugs. Tetracycline 3% is active ingredient in each of the products other than VenomX with zinc acetate 0.1 % by volume (*see box*).

Additionally, the four products are mislabeled because they are "offered for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, adequate directions cannot be written so that a layman can use the products safely for their intended uses," officials said.

NOT A TYPICAL OTC FIRM

In addition to claims rarely found for products made with OTC monograph drug ingredients, other characteristics of Phillips' operations set it apart from typical nonprescription drug manufacturers.

For instance, packaging for Phillips' four products, pictured here, lacks the color and imagery typically used on OTC drug packages.

Although it is looking for a buyer, the firm pledges on its website that "what was impossible can often become possible" in support for President Trump's Feb. 28 statement about FDA: "Our slow and burdensome approval process … keeps too many advances from reaching those in need. If we slash the restraints, not just at the FDA but across our Government, then we will be blessed with far more miracles."

And there are Phillips' claims questioned by FDA, including, with product labels linked:

- **Tetracycline-ABC** "Kills MRSA, Staph (Staphylococcus aureus), Acinetobacter baumannii, Acinetobacter lwoffi, Klebsiella pneumoniae, E. coli, Proteus vulgaris, Pseudomonas aeruginosa, Enterobacter cloacae, and Group-A strep";
- For both **Diabecline** and **TetraStem**, "With only a TOPICAL (rub-it-on-the-skin) formula, it is now possible to successfully induce stem cell therapy to treat spinal cord injury and dramatically reduce paralysis";
- "**VenomX** is an anti-venom cleanser formulated to chemically attack and dissolve the snake venom rapidly, rendering it less harmful."

MICROBIAL TESTING MISSING FOR ANTISEPTICS

The GMP problems found at Phillips' facility included not having, for each batch, appropriate laboratory determination of satisfactory conformance to final specifications for drug products. Specifically, it lacked testing for microbial attributes, including absence of objectionable microorganisms, or sterility.

"We note that your topical antiseptic drug products are indicated for use on injured skin, minor cuts, scrapes, and burns. It is essential that your drug products are tested for appropriate microbial attributes in view of their intended uses," ORA officials said.

Phillips GMP problems also include failing to:

- use equipment constructed to ensure surfaces that contact components, in-process materials or drug products are not reactive, additive, or absorptive so as to alter the safety, identity, strength, quality or purity of the product;
- establish adequate written responsibilities and procedures applicable to its quality control unit;
- test samples of each component for conformity with all appropriate written specifications for identity, purity, strength, and quality;
- establish written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess;
- prepare batch production and control records with complete information relating to the production and control of each batch of drug product.

"Our findings demonstrate a lack of understanding of the basic elements of a compliant manufacturing operation, such as suitable facilities and equipment, trained personnel, appropriate components, a well-defined process, and written procedures," the warning states.

The firm did not respond to comment following requests left with Howard Phillips LLC in Arizona and with Mr. Phillips personal line. Phillips Co.'s Oklahoma facility could not be reached. Its website documents are not dated, but appear to have been updated in 2017.

The letter to Phillips, which FDA published May 16, marks a rare warning to an OTC drug manufacturer. Although FDA within the past five years conducted enforcement that led to consent decrees temporarily slowing or shutting down OTC manufacturers' operations, it submits warning letters much more frequently to firms operating other areas of its oversight – Rx drugs, dietary supplements, cosmetics, and food, tobacco and veterinary products. *(Also see "FDA GMP Warning Letters Review: Rate Soared In 2016 On Sterility And Data Integrity Concerns" - Pink Sheet, 25 Apr, 2017.)*

J&J Settlement With States Not Likely To Be Precedent In OTC Space

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The factors leading to **Johnson & Johnson**'s $33m settlement with 42 states on GMP-related issues for consumer products are unlikely to combine again, lessening chances that the agreement is a sign of things to come for others in the consumer health space.

Those factors include the prominence of the company and use of an FDA consent decree even though no adverse events were reported for the products involved.

The firm's widespread good manufacturing practices problems prompted recalls and led to a 2011 consent decree with FDA to remediate its headquarters OTC drug plant and two others *(see box below)*. However, state attorneys general followed up with their own enforcement actions, including efforts to penalize the company for potential harm to consumers from products sold prior to the recall.

The agreement between J&J and attorneys general from the states plus Washington, D.C., was initially announced May 24 by New York Attorney General Eric Schneiderman (D) and acknowledged the next day by J&J.

In addition to the financial payment, the settlement prohibits the firm's consumer products business from advertising on its websites that its OTC product facilities meet FDA's GMP requirements in cases where a drug has been the subject of a class I or II recall within the previous 12 months.

Class I recalls involve a reasonable probability that use or exposure may result in serious detrimental health consequences or death; class II recalls involve potential temporary or reversible health consequences, or where potential adverse health consequences are unlikely. None of J&J's recalls covered in the agreement were class I, several were class II and most were class III, a violative product not likely to cause adverse health consequences.

Additionally, J&J is precluded from posting any online banners saying it is GMP-compliant should it fail to follow internal operating procedures about corrective or preventive actions for OTC drugs during manufacturing, or to identify or provide information to participating state AGs within 60 days of a written request about vendors or warehouses where recalled OTC drugs were distributed in their states.

In a statement to the Pink Sheet, J&J pointed out the recalls of *Tylenol*, *Motrin* and other OTC brands it conducted prior to the consent decree with FDA were "were precautionary and not undertaken on the basis of any health or safety risks to consumers."

The firm said it is "pleased to finalize a settlement agreement … related to the manufacturing of certain over-the-counter products that were recalled voluntarily between 2009 and 2011."

'GIANT LEAP' FROM GMPS TO HARM

The settlement not only is the final step in J&J's negotiations with Schneiderman and the other state AGs, it also could mark the only instance of an alignment of all the factors that put the firm in the state agencies' cross-hairs:

- few if any firms are better known than J&J in the US consumer health space;
- its lineup of iconic OTC brands is unsurpassed;
- its widespread recalls, with no adverse event reports about the products, did not deter FDA from imposing the decree for remediation, a rarity in the OTC sector;
- its GMP problems surfaced after J&J significantly expanded its operations in its 2006 acquisition of **Pfizer Inc.**'s previous consumer health business *(Also see "J&J Bit Off More Than McNeil Could Chew In 2006 Pfizer OTC Acquisition" - Pink Sheet, 31 Oct, 2014.)*;
- J&J also pleaded guilty in Pennsylvania federal court to a charge linked to failing to have a Corrective Action Preventive Action (CAPA) at one of its plants.

All those factors – from J&J's marketplace prominence to its guilty plea – aren't likely to combine again and put a consumer health product firm under the thumb of state authorities pushing to recover damages based on FDA's enforcement of its regulations.

Not only are consent decrees requiring facility remediation rare in the consumer health sector, so are occasions of consumers being harmed from use of products manufactured at facilities where FDA finds GMP problems.

"In most situations, GMP violations don't harm anybody," said Pete Mathers, a food and drug law attorney and a partner at Kleinfeld, Kaplan and Becker LLP in Washington.

"The facts were relatively extreme, including the criminal guilty plea. It was rather like some of the widespread food contamination cases, though with less established consumer harm. There may not be many such easy cases for them to jump on," said a second food and drug attorney.

Tort attorneys, not to mention state attorneys general, would be hard-pressed to link consumer harm to a GMP problem that FDA officials note about OTC drug or dietary supplement facilities in their form 483 findings or in warning letters sent to firms that fail to sufficiently respond to those findings.

A form 483 or a warning letters is not "a legal binding finding of any sort," said Mathers. "To claim you are being harmed in any way [by a GMP problem] is a significant leap," he added.

Similar problems have been reported by other OTC drug firms, but none amounted to the combination of FDA, DoJ and state agency enforcement J&J has endured. FDA inspectors found CAPA problems at **Perrigo Co. PLC**'s Allegan, Mich., facilities and submitted a warning letter in 2010, but the agency did not enforce further. *(Also see "Perrigo Applies Crime Scene Investigation Model To Improve Quality Control" - Pink Sheet, 17 Oct, 2011.)*.

Novartis AG's exit from being active in the consumer health sector in 2015, by

'PHANTOM' RECALL TO CAPA

J&J, which changed its consumer business' name from McNeil Consumer Health to Johnson & Johnson Consumer Inc. in 2016, agreed to the decree following an investigation prompted by a string of recalls in 2009 and 2010 of OTC products in the Tylenol, Motrin, Zyrtec and Benadryl lines, including children's products.

Its Fort Washington, Pa., manufacturing facility was closed until after an independent expert conducted an audit and FDA determined the site was GMP-compliant. The firm's Las Piedras, Puerto Rico, and Lancaster, Pa., plants also were audited, but allowed to continue operating. *(Also see "J&J/McNeil Completes Remediation Under Consent Decree" - Pink Sheet, 7 Sep, 2015.)*

The largest impact from recalling the products was a $900m bite out of J&J's fiscal 2010 sales. A big piece of the recalls, more than 53m products, was due to a moldy odor from a chemical used on the wood pallets used to store the products at the Las Piedras plant. While other reasons for the recalls included mislabeled products and reports of foreign substances found in products, J&J also conducted a "phantom" recall of a Motrin SKU by attempting to buy up retailers' stocks without informing consumers or FDA. *(Also see "J&J Delivers No Evidence FDA Knew Of "Phantom" Recall - Congressional Staff" - Pink Sheet, 27 Sep, 2010.)*

In 2015, J&J entered a guilty plea in federal court in Philadelphia and agreed to pay a $20m fine and forfeit $5m for a misdemeanor count of delivering into interstate commerce adulterated liquid OTC drugs from its Fort Washington plant. *(Also see "Missing CAPA Costs J&J $25 Million In Investigation Sparked By OTC Recalls" - Pink Sheet, 11 Mar, 2015.)*

shifting its brands to a joint venture operated by **GlaxoSmithKline PLC**, came after widespread problems at its US plants, but without a consent decree or state enforcement actions. *(Also see "Glaxo In Charge, And The World Is GSK/Novartis Consumer Product JV's Oyster" - Pink Sheet, 8 Jun, 2015.)*

Schneiderman and other state AGs, however, have brought enforcement actions against supplement manufacturers that led to settlements on allegations of marketing adulterated products in their states, and an investigation by the New York AG's office led to **GNC Holdings Inc.** agreeing to a settlement that imposed quality-control requirements not imposed under FDA's GMPs. *(Also see "GNC Targets 'Consumer Trust' In N.Y. Agreement, But Industry Wary Of Impact" - Pink Sheet, 15 Apr, 2015.)*

Still, when state agencies wield enforcement in drug or supplement manufacturing, they are working with federal regulations that FDA enforces according to guidance it publishes for the industries.

"FDA enforces GMPs and FDA defines what GMPs," Mathers said. Understanding those definitions to achieve and maintain compliance are something "manufactures struggle with all the time," he said.

The states that are not part of the settlement are Alabama, Georgia, Iowa, Mississippi, Oklahoma, Oregon, Utah and Wyoming.

'Do Not Flush' Labels For Acne, Hemorrhoid Wipes Won't Stop Consumers – CHPA

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The Consumer Healthcare Products Association and other opponents of "do not flush" labeling requirements for nonwoven disposable wipes hope a recent labeling rule passed in Washington, D.C., does not augur similar rules in other areas of the US.

The regulation, the "Nonwoven Disposable Products Act of 2016" (Act 21-604), passed in D.C. and scheduled to take effect in January, is similar to legislation in Maryland, Minnesota, New Jersey and New York and a pending New York City ordinance that seek restrictions or requirements for labeling the wipe products.

According to the requirements of the regulation the D.C. City Council enacted in March, disposable wipes for acne and hemorrhoids as well as other personal care wipes made of nonwoven disposable material that does not meet the act's definition of "flushable" will not be available in the city starting in January unless labeled with "do not flush" on packaging.

CHPA President and CEO Scott Melville highlighted opposition to wipes labeling legislation among the trade group's 2017 priorities at the CHPA Annual Executive Conference in Amelia Island, Fla., in March . He warned that companies marketing acne or hemorrhoid wipes could be impacted. *(Also see "OTC Monograph Reform, User Fee Legislation Coming 'Any Day' – CHPA" - Pink Sheet, 30 Mar, 2017.)*

The D.C. bill, which became law following a 30-day congressional review, is intended is to prevent clogs in the city's wastewater system. The Washington Suburban Sanitary Commission, which handles sewage in the city and large swath of the its suburbs, spent $1m on grinding machines to destroy a disrupting build-up of wipes and other paper products in the sewer system, according to media reports.

The act prohibits, starting in January, manufacturers of nonwoven disposable wipes sold in D.C. from labeling the products "as safe to flush, safe for sewer systems, or safe for septic systems, unless" they are flushable.

It states that "flushable" is a "nonwoven disposable product" that "disperses in a short period of time," "is not buoyant" and "does not contain plastic or any other material that does not readily degrade in a range of natural environments."

> Starting in 2018 in Washington, D.C., acne and hemorrhoid wipe manufacturers "must clearly and conspicuously label the nonwoven disposable product to communicate that the nonwoven disposable product should not be flushed."

The act defines "label" as to "represent by statement, word, picture, design or emblem on the packaging of a nonwoven disposable product" and defines "nonwoven disposable product" as an item "constructed from nonwoven sheets, including moist toilet tissue or cloth, that is designed, marketed, or commonly used for personal hygiene purposes."

Further, manufacturers "must clearly and conspicuously label the nonwoven disposable product to communicate that the nonwoven disposable product should not be flushed."

Manufacturers that do not comply will face civil fines and penalties or sanctions, and the city may seek injunctive relief or "other appropriate remedy in any court of competent jurisdiction to enforce compliance with this act," the law states.

Products the act targets include **Pfizer Inc.'s** *Preparation H* Medicated Hemorrhoidal Wipes, **TargetCorp.**'s store brand *Up&Up* Medicated Wipes and **Wal-Mart Stores Inc.**'s store brand *Equate* Flushable Hemorrhoidal Medicated Wipes. All the hemorrhoid products, which are regulated as cosmetic products, contain witch hazel and all packages currently bear a "flushable" and/or "septic safe" claim.

Wipes for acne contain either OTC drug monograph acne-fighting ingredients or natural extracts and most are not labeled "flushable" on packaging. The products include **Valeant Pharmaceuticals International Inc.**'s *AcneFree* wipes with salicylic acid and **Johnson & Johnson**'s *Neutrogena* cleansing wipes with grapefruit extract.

The rule also targets product categories including flushable baby wipes, adult personal hygiene wipes as well as those not advertised as flushable.

LABELING NOT THE ISSUE - CHPA

Opponents of the D.C. rule and similar legislation in other states say the problem with sewage buildup is due to consumers flushing wipes intended for the trash. They say if firms no longer distribute flushable wipes to states or other jurisdictions due to rules similar to D.C.'s, many consumers will turn to plastic-embedded, non-flushable baby wipes for purposes they currently use nonwoven flushable wipes. An absence of nonwoven wipes would compound sewer system blockage because plastic-embedded products do not disintegrate and collect with similar materials into blocks that must be removed.

Opponents also note a New York City independent study at its Wards Island wastewater treatment plant that found that products legitimately marketed as "flushable" account for 2% of plant clogs. The remainder of the clogging material is form consumer improperly flushing other items not intended to be flushed, such as paper towels and non-flushable baby wipes.

Emphasizing the New York study in a 2016 release, INDA said it partnered with the National Association of Clean Water Agencies to reduce the burden of non-flushable

disposable products in the wastewater system. NACWA Director of Regulatory Affairs Cynthia Finley noted problems in sewer systems are caused by flushing products that don't disintegrate in the sewer system, including baby wipes, personal care wipes, paper towels and feminine care products.

"These products are sometimes disposed of in toilets because of how and where they are used, causing significant economic burdens on local wastewater treatment systems," Finely said.

INDA also emphasized many firms already follow industry standards, thanks to its guidelines for wipe "flushability." Most recently updated in 2013, the guidance provides INDA members with a code of practice for labeling products as flushable or not. The guidelines also define product qualities that necessitate a "do not flush" label.

INDA guidelines says "flushability" is appropriate if a product:

- "clears toilets and properly maintained drainage pipe systems when the suppliers' recommended usage instructions are correctly followed";
- "passes through wastewater conveyance systems and is compatible with wastewater treatment, reuse and disposal systems without causing system blockage, clogging or other operational problems";
- "is unrecognizable in effluent leaving onsite and municipal wastewater treatment systems and in digested sludge from wastewater treatment plans that are applied to soil."

NEW YORK CITY PROPOSAL

Similar legislation (Intro. No. 666) was introduced in New York City in 2015 and is pending review by the city's Environmental Protection Committee, according to a city legislative website.

The bill would make it unlawful to "sell or offer for sale a nonwoven disposable product whose packaging indicates that such product is flushable unless such product satisfies the definition for flushable" in the bill and "complies with testing standards established by the commissioner of environmental protection through rulemaking."

Additionally, it would prohibit the "sale or offer for sale a nonwoven disposable product that does not satisfy the definition for flushable…unless the packaging of such product indicates that such product is not flushable." Retailers violating the regulation law would face a civil penalty of up to $2,500.

New York state legislators in January introduced legislation in the state Senate (S2901) and Assembly (A3698) to amend the state's general business law to prohibit labeling or advertising a nonwoven disposable product for sale as flushable without approval from the state. The law would take effect 90 days after enactment.

The legislation, in committee review in both chambers, excludes media and wholesalers or retailers that distribute or sell but do not package or label a nonwoven disposable product advertised, packaged or labeled as flushable or safe for sewer or septic. It says each violation of the law could draw a fine of up to $5,000.

The Maryland Senate passed SB 280 in March to prohibit advertising or labeling of nonwoven disposable products as safe to flush or for disposal in sewerage systems or septic systems unless the product meets the bill's definition for flushable: "disperses in the low-force conditions of a sewage system a short period of time after flushing, is not buoyant and does not contain plastic or any other material that does not readily degrade in a range of natural environments."

A version of the bill also was introduced into the House in March and was referred to the Interim study by Economic Matters.

If enacted, the law would take effect in January, requiring manufacturers to clearly and conspicuously label such a product in a manner that alerts the purchaser that a product should not be flushed.

In Minnesota, companion bills in the Senate (SF 2040) and House (HF 2292) have been referred to committee. Similar to the other state bills, the proposals would prohibit labeling or advertising nonwoven disposal product as flushable or septic or sewer safe unless it meets a definition stated in the legislation: "meets the tests for flushability established by the [Federal Trade Commission] for non-misleading representations regarding the flushability of nonwoven disposable products, or that complies with the most recent INDA code of practice for product labeling" approved by the state Pollution Control Agency."

The bill also would levy a $100 civil penalty for each pre-packaged salable unit offered for sale, with a $5,000 maximum.

For New Jersey's 2016-2017 session, A3218 states similar prohibitions for nonwoven disposable product labeling and was introduced in February 2016 but has remained in the Environment and Solid Waste Committee. No companion bill has been introduced in the state Senate.

Additionally, FTC is pushing to persuade marketers from advertising products as flushable unless they are proven to be. In 2015, FTC approved a final consent order that prohibits **Nice-Pak Products Inc.** from marketing its moist toilet tissue and cloths as flushable or safe for sewers systems unless it is able to provide substantiation for the claims.

Petition Seeks OTC PPI Warning On Cancer Risk From Persistent Heartburn

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FDA is being asked to add yet another safety warning to OTC proton pump inhibitors. A citizen petition requests requiring a label warning on the risk of esophageal cancer from persistent heartburn, a risk not lessened by PPI use.

"The warnings on current products are not sufficient to alert patients to the risk of esophageal cancer associated with persistent heartburn resulting from reflux disease, acid indigestion or sour stomach," states Esophageal Cancer Action Network Inc. in a May 1 petition to the agency.

ECAN President Mindy Mintz Mordecai and Chairman John Lipham explain in the petition that because PPIs are effective in providing symptomatic relief, many patients likely do not seek medical intervention for the persistent heartburn that can lead to Barrett's esophagus – a precancerous condition that causes as much as a 125-fold increase in the chance of developing esophageal cancer.

The nonprofit group points out that about 15m US consumers experience heartburn daily, and about 3m currently have Barrett's esophagus, with more than half of those unaware they have the condition because it presents no symptoms. Esophageal cancer often is only discovered when it has reached advanced stages when treatment outcomes are poor.

"In our view, the inclusion of a bold, prominent and strong warning will serve to better inform patients of the risks associated with persistent heartburn and the need to see their physician due to the risk of esophageal cancer that can go undetected if the patient is getting symptomatic relief from the OTC drug products," ECAN said.

PPIs available OTC in the US include the category pioneer *Prilosec OTC* (omeprazole 20mg) marketed by **Procter & Gamble Co.**under license from innovator **AstraZeneca PLC**;**Bayer HealthCare LLC**'s *Zegerid OTC* (omeprazole 20mg); *Prevacid 24HR* (lansoprazole 15mg) marketed by **GlaxoSmithKline Consumer Healthcare LP**; the latest category entrant *Nexium 24HR*(esomeprazole 20mg)marketed by **Pfizer Inc.**, also under license from AstraZeneca**;** and private label versions of all those brands other than Nexium 24HR.

DIARRHEA, DRUG INTERACTION FEARS PREVIOUSLY NOTED

Researchers and public health advocates previously convinced FDA to require PPI label changes concerning different safety risks.

In 2014, FDA published several drug safety communications and began work with PPI marketers on label changes in response to a 2011 citizen petition by Public Citizen. The safety communications included risks of Clostridium difficile-associated diarrhea from PPI use and drug-drug interactions with pharmaceutical drugs clopidogrel, methotrexate and mycophenolate mofetil. *(Also see "Public Citizen Urges FDA To Add Sweeping Warnings To PPI Labels" - Pink Sheet, 29 Aug, 2011.)*

FDA said it would work with firms to add clopidogrel-interaction information on labels for all Rx and OTC PPIs containing omeprazole and esomeprazole.

'BOLDER' CANCER RISK WARNINGS NEEDED

ECAN argues that OTC PPI label warnings should include a "stronger, bold and prominent" statement on the risk of potential esophageal cancer and noting that the products do not eliminate the risk. The existing label warnings on PPI products state:

- Your heartburn continues or worsens
- You need to take this product for more than 14 days
- If you need to take more than 1 course of treatment every 4 months"

ECAN suggests replacing those warnings with these:

"Persistent heartburn can indicate increased risk of developing esophageal cancer."

"This medication will not eliminate that risk. Ask a doctor before use if you have:

- Had heartburn over 3 months. This may be a sign of a more serious condition."

"Stop use of the product and see your physician

- If your heartburn continues or worsens; or
- If you need to take this product for more than 14 days; or
- If you need to take more than 1 course of treatment every 4 months."

Returns From Sanofi Consumer Expansion Could Point To More

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Sanofi's launch of *Xyzal Allergy 24HR* in the US helped remedy its slumping consumer health product business with more than $43m sales in the first quarter as the division's overall revenues grew nearly 5% to $1.5bn.

The French pharma's strategy of driving consumer health business growth by expanding the product lineup played out during the first quarter not only with the launch of OTC switch Xyzal Allery, but also with further integration of OTC drug and vitamin brands recently acquired from **Boehringer Ingelheim GMBH**. Company execs said they are looking to further strengthen the consumer business, including through potential acquisitions and Rx-to-OTC switches.

During Sanofi's April 28 earnings briefing, CEO Olivier Brandicourt said the Xyzal launch "enhanced" revenue growth for the consumer product business, which he claims "now ranks as the leading global player" in consumer health care products.

Additionally, an early and strong cough and cold season in Europe helped drive sales growth for the unit. There also was improvement from some emerging markets, but that sector "is still not where we want it to be, mainly due to the tough economic environment in Russia," Brandicourt said.

Alan Main, Sanofi's executive vice president for consumer products, suggested Xyzal results could improve during the current quarter, noting that the product "was just getting in its pipeline fill into the retail sector at the end of the first quarter."

Main added, though, that the US allergy season might not create high demand for Sanofi's and other firm's products. "It's obviously a bit too early to indicate there, although the first signs of allergy season in the US. are relatively weak. But we're not near the peak season yet, which comes in the next 2 or 3 weeks," he said.

Like Brandicourt, Main described Sanofi's integration of Boehringer Ingelheim's product lines as on track since the January closing its acquisition of privately held BI's consumer products business, excluding China,

Sanofi expanded is US OTC lineup during the quarter with the Xyzal Allergy launch, which also put the firm in the pediatric 24-hour allergy treatment competition.

SANOFI'S 1Q 2017 IN BRIEF

Group sales:
€8.6bn, up from €7.8bn in 1Q 2016

EPS: €1.42

Global sales for diabetes products:
€1.7bn, down by 6% from 1Q 2016

Global sales for rare disease products:
€712m, up 8% from 1Q 2016

Global sales for MS drugs:
€496m

Global sales for oncology products:
€412m, up 13% from 1Q 2016

and €4.7bn ($5.2bn) in exchange for Sanofi's **Merial** animal health business. *(Also see "Sanofi CEO Sets Growth Target For Consumer Health Business" - Pink Sheet, 30 Oct, 2016.)*

"We saw no business disruption in the first couple of months of operation," Main said, adding that Sanofi expects to achieve synergy targets it identified in the deal.

The firm's overall net sales grew 11.1% on a reported basis to €8.65bn ($9.45bn). Led by the Xyzal Allergy launch, its US consumer business sales grew 2.4%, or 18.7% when including BI's products, to €348m ($380.1m). Along with Xyzal, Sanofi's *Allegra Allergy* (fexofenadine hydrochloride) line helped drive Sanofi's OTC allergy and cough/cold lineup to 12.9% growth.

Sales of Sanofi's OTC, vitamin and personal care brands slipped 1.2% to $2.6bn for full-year 2016 after ending the year with 2.7% fourth-quarter growth to $890.3m following decreases during the first three quarters, including a 4.3% dip during the April-June period. *(Also see "Sanofi's Consumer Business Starts 2017 With 'Reassuring' Momentum" - Pink Sheet, 9 Feb, 2017.)*

'WE WOULD BE OPEN' TO MORE CONSUMER DEALS

The BI deal, Brandicourt acknowledged in response to analysts' questions, might not be the end of Sanofi's deal-making to grow its consumer products business. Consumer health care is on the table for expansion through mergers or acquisitions as a "treatment area" in which Sanofi already claims some market-share leadership, the CEO said.

Results during the January-March period show the BI acquisition is "working well," but don't represent the end of consumer health expansion for Sanofi, he said. "Does that mean that in the mid-term or longer term, we wouldn't look at eventually strengthening even further this business? Of course not. So, we would be open."

Consumer health is among the areas "we wanted to strengthen. We have done definitely a very important step there. But it might

not be the end of the story and opportunities will be critical or will determine the future of that aspect," Brandicourt added.

In addition to M&A, Rx-to-OTC switches are part of Sanofi's tool kit for growing its consumer business, with the first-quarter launch of Xyzal Allergy 24HR its latest introduction of a new ingredient in the nonprescription space.

FDA in January approved a new drug application to switch its Xyzal Rx allergy treatment to OTC in 5 mg tablets indicated for children 6 and up and adults and in a 2.5 mg per 5 mL "Tutti-Frutti" flavor oral solution, indicated for children 2 and up as well as older children and adults. Sanofi already competed in the OTC antihistamine market with Allegra Allergy, but the fexofenadine hydrochloride line currently is limited to a 12-hour product for children while other nonprescription antihistamine brands such as Claritin and Zyrtec and private label versions of those already offered 24-hour formulations for children. *(Also see "Xyzal Switch Extends Sanofi Into OTC 24-Hour Children's Antihistamine" - Pink Sheet, 2 Feb, 2017.)*

Also in Sanofi's OTC switch plans is potentially the first erectile dysfunction treatment to be available nonprescription in the US. It has exclusive rights from innovator **Eli Lilly & Co.** apply for *Cialis* OTC approval in the US, Europe, Canada and Australia. Cialis (tadalafil) is available Rx in the US in 2.5-, 5-, 10- and 20-mg doses and can be used as needed or once daily. *(Also see "Cialis Or Viagra Switch? Sanofi Survey, Pfizer Help Wanted Ad Could Be Signs" - Pink Sheet, 18 Nov, 2016.)*

Sanofi stated in August that it was talking with FDA about submitting an NDA for a Cialis switch. The firm did not respond a May 1 request for comment to update the switch initiative.

Market analysts emphasized concern for Sanofi's outlook in the diabetes treatment space, but some also noted the consumer unit's contribution to its earnings.

Morningstar's sector director, Damien Conover, said in a same-day research note that he considers Sanofi's stock "undervalued" because he "investment community appears overly focused on the challenges in the diabetes group." Consumer health care, on the other hand, along with Sanofi's specialty care and vaccines businesses are not getting enough credit for the firm's "solid positioning," he said.

Conover also noted that comparisons to the year-ago quarter are complicated by Sanofi's deal with BI and the end of is vaccine joint venture with Merck, but he expects "the stronger entrenchment in consumer health care will enable the firm to more efficiently market the product portfolio."

Sanofi's share price on the Nasdaq exchange bumped up when it released its first-quarter results, from the previous day's close of $46.83 to $47.44 in early trading on April 28, and after leveling off later that day, have continued climbing to as high as $48.15 on May 2.

Perrigo Consumer Results' Significance Grows With Tysabri In Past

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Perrigo Co. PLC's restating of several years of financials drives home the point that its primary sales driver is consumer health care products while encouraging investors enough to maintain a recent share price increase after an extended slump.

The US private label OTC market leader restated earnings reports for its fiscal years 2014 and 2015 and filed with the Securities and Exchange Commissioner amended 10-Q reports on its earnings for the first, second and third quarters of 2016.

On May 22, the firm – which also markets OTC drugs and nutritional products in Europe and Latin American markets and manufactures Rx specialty topicals and active pharmaceutical ingredients –said it revised its historical financial statements to reclassify revenues from its now-divested license for *Tysabri (*natalizumab) multiple sclerosis treatment royalties, garnering tax benefits for those periods (benefits that will not continue given the sale of the product).

Perrigo reviewed historical revenues from Tysabri royalties, a license it sold to **RPI Finance Trust** for $2.85bn, including $650m in contingent milestones, in a deal that closed in March. *(Also see "Perrigo Trims Workforce, Ships Tysabri License, Stays European Course" - Pink Sheet, 1 Mar, 2017.)*

The royalty stream reporting shift decreased Perrigo's 2015 net sales by around $3m while adjustments in taxable revenues for its European consumer health business increased the unit's net income by around $19m and raised its tax expense around $15m. The firm said the net effect of other non-Tysabri adjustments in 2016 was an increase of around 2 cents in its adjusted diluted earnings per share.

During a May 23 briefing with analysts, CEO John Hendrickson the firm's "durable business model continues to be led by our consumer-facing business."

The consumer health business, which includes animal care products, accounts for around 80% of Perrigo's consolidated net sales, which were adjusted to $5.2bn in 2016 on operating income of $1.1bn with adjusted earnings per share of $5.07.

2017 Q1 RESULTS STILL PENDING

Perrigo, based in Dublin while maintaining its primary operations in the Allegan, Mich., area, delivered the restated financial information within a month of launching the review, but has yet to say when it will publish sales results for the 2017 first quarter.

Acting Chief Financial Officer Ronald Winowiecki said during the briefing that Perrigo's "accounting team continues to march on with an intensive plan to complete our first quarter 2017 Form 10-Q filing as soon as practical."

So far, Perrigo has reported interim, unaudited first-quarter results of consumer health product sales of $580m in North and Latin America sales and $370m in Europe, Rx generics sales of $220m and net sales of around $1.2bn, in line with its forecast.

Meanwhile, analysts say divesting the Tysabri royalty license still leaves Perrigo vulnerable in the Rx generics arena, where pricing pressures look likely to worsen with continued consolidation among purchasers.

"The reality is the consumer business needs to improve," said Jefferies Equity Research Americas analysts in a May 23 research note.

However, while Perrigo's OTC drug product launches look stronger for 2018, "the size of the OTC pipeline remains unclear and it's uncertain if pricing headwinds will abate in the near to medium term," Jefferies analysts said.

BTIG Equity Research analysts also advise caution about Perrigo's near-term results, and note they "think it's still unclear whether [the firm] PRGO keeps its Rx pharma segment."

Lowering its debt load "have likely been expedited" with proceeds from the Tysabri deal, but BTIG analysts say we believe a turnaround for [Perrigo] will take time, as pricing headwinds remain in" 2017, according to a May 22 research note.

Deutsch Bank analysts' also credit Perrigo for lowering its debt while giving a nod to the firm's confidence. "We take comfort in management's comments that the fundamentals of the remaining business units are stable," the analysts' said in a May 23 research note. They added that Perrigo "management believes [the firm's] competitive advantages in consumer healthcare remain strong."

Perrigo offered its first fiscal 2017 guidance on earnings per share, $4.15 to $4.50, excluding Tysabri royalties, and adjusted its operating income guidance to between $930m and $990m.

Its forecast of around $2.4bn for consumer health Americas segment full-year net sales includes an impact from a strong cough and cold season in the first quarter and assumptions for an average allergy season.

Perrigo forecasts around $1.4bn in international consumer business sales on OTC growth of roughly 2%, consistent with the overall market, and on savings of around $210 million from exiting its European distribution businesses.

The firm's share price climbed from $71.30 to $73.53 the day of its earnings update release before returning to between $72.54 and $70.41 from May 23 through mid-day May 26.

Perrigo shares were trading at $198.70 in April 2015 when **Mylan NV** made an unsolicited acquisition tender of $75 cash and 2.3 Mylan shares. The share price varied between around $200 and around $180 through mid-September that year but began a steady slide that was down to $146.90 when Mylan's tender failed and until recently continued falling as the firm missed sales forecasts while struggling to turn its European consumer health business into a profitable operation. *(Also see "Perrigo's Return To OTC Roots Restoring Investor Confidence" - Pink Sheet, 1 May, 2017.)*

Coppertone 'Assurance Assessment' Anticipates Criticism From Sunscreen Reviews

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Bayer AG gets in front of consumer advocacy groups' annual sunscreen product rankings and shopping recommendations with an independent review of label claims for its *Coppertone* line.

The German firm's US consumer health product business recently released a consultant's "assurance assessment" intended to bolster consumer confidence in Coppertone labeling, countering advocacy groups' criticism that the industry sees as often based on hazily defined testing approaches and contentious ingredient safety positions.

"Consumers are receiving information about sun protection from a variety of often contradictory sources, which is causing confusion. They want assurance that product performance claims are based on legitimate scientific testing," said Michael Tune, vice president at Bayer consumer's personal care development center.

"As a leader in the US sun care industry, we wanted to utilize our long-standing leadership to meet the changing expectations of consumers by voluntarily conducting – and sharing – this independent assurance assessment," he added in an April 24 release.

Bayer commissioned global consulting and standards firm AccountAbility to audit the firm's internal processes, systems, controls, performance guidelines and associated data that inform its sunscreen labeling, focusing specifically on 10 top-selling Coppertone products in the US.

According to Eduardo Ruvolo, director of US and international medical affairs for sun and skin care products, the results show that Coppertone products "consistently and reliably provide the level of sun protection that our consumers expect and trust us to deliver."

That aspect of the assessment could serve as a proactive defense against any pending allegations from Consumer Reports, which has issued findings over the past four years suggesting many sunscreen products on the US market do not deliver on their SPF promises. *(Also see "PCPC Scorches Consumer Reports Test Methods In Assessing SPF Claims" - Pink Sheet, 25 May, 2015.)*

While Coppertone Water Babies SPF 50 was among products that made the Consumers Reports' "recommended" list in 2016, industry generally has questioned Consumer Reports' testing methods, and brands in past years have been compelled to retest products, verify challenged SPF claims and reassure their customer bases.

AccountAbility also deemed Coppertone compliant with FDA's testing and labeling guidelines, as well as relevant international standards for product safety, efficacy and quality assurance, Bayer says.

The consulting firm reached its conclusions after reviewing the firm's product development and manufacturing quality-assurance procedures in the US for the 2016

period, with access to Bayer/Coppertone facilities, records and personnel.

It specifically combed through documentation for 10 selected Coppertone spray, lotion and stick products, as well as the brand's new "whipped" formulations. *(Also see "Coppertone Innovates With Texture, Launching 'Whipped' Sunscreens" - Rose Sheet, 7 Apr, 2017.)*

The review considered data from the company's final formulation testing – and the sun protection factor, water resistance, stability and broad-spectrum claims constructed around those test results – assessing against US and international standards.

AccountAbility also examined Bayer/Coppertone's internal supplier audit processes and controls and performance metrics for third-party testing labs and contract manufacturing organizations, among other elements of its operations.

The consulting firm notes it did not test or re-test Coppertone sunscreen products.

However, "nothing has come to our attention that causes us to believe that Bayer has not [for the 2016 period] complied, in all material aspects, with its internal guidelines designed to ensure the quality, safety and efficacy of the products."

Further, the company's records overwhelmingly affirm that it "accurately tested and implemented quality assurance procedures, based on its reasonable interpretation of market regulation for the United States," to ensure the accuracy of its labeling claims, AccountAbility says.

The firm notes that at the time of its report, Bayer, which acquired Coppertone in 2014, still was locating results from FDA-required critical wavelength testing conducted by the brand's former owner, **Merck & Co. Inc.** The missing test results – to support broad-spectrum protection claims – pertain to a single selected "legacy" product sample, according to the report.

Coppertone's recently launched Whipped sunscreens, including Clearly Sheet, were included in AccountAbility's audit of internal processes, systems, controls, performance guidelines and associated data that inform Bayer's sunscreen labeling.

"Bayer's archiving of testing results conducted by Merck is part of an on-going post-integration process. Once located, Bayer will formally archive the testing results in its central file depository system and, once provided, AccountAbility will update this report," it says.

Among the firm's recommendations for Bayer is "improving documentation references for easier access to records."

EWG SCORE NOT LIKELY TO IMPROVE

The independent assessment may not offer defense against another NGO report that tends to command significant consumer attention on an annual basis – the Environmental Working Group's Guide to Sunscreens – which has included Coppertone products in previous years' "worst" lists based on ingredient concerns that industry says are unwarranted and labeling practices permitted by FDA.

Overall, EWG rates the Coppertone brand a 3-10 (moderate to high hazard) on its Skin Deep scale.

Specifically, EWG has faulted the brand for using oxybenzone, which it links to hormonal effects and sensitization risks, and antioxidant retinyl palmitate, which the group maintains can have carcinogenic effects when exposed to sunlight. Industry refutes such assertions based on the bulk of available scientific evidence.

Moreover, EWG marks down Coppertone for labeling sunscreen products with SPFs higher than 50.

FDA is examining whether to cap SPF values at 50+ due to concerns that high-SPF products may give consumers an inflated sense of confidence that is not proportionate to the incremental clinical benefit that such offerings provide. However, industry members have contested those assumptions, and the agency is still considering stakeholder comments on what currently is only a proposed rule. *(Also see "FDA Considers Capping SPF Values At 50+ Despite Efficacy Data" - Pink Sheet, 20 Jun, 2011.)*

Even if the AccountAbility report doesn't earn Coppertone points with EWG in those departments, the investment could prove a savvy one, serving as an authoritative marketing asset and a ready exhibit for the brand to point to if it comes under fire from detractors.

In the digital era, with a growing premium on consumer trust, NSF International is looking to provide a similar independent vetting service to cosmetics firms concerned about "consumer assurance." *(Also see "NSF International Launches Cosmetic Verification Program For 'Consumer Assurance'" - Rose Sheet, 18 Apr, 2017.)*

"Coppertone has continued its commitment to quality, excellence, innovation and truth in labeling, backed up by science, clinically relevant data and robust testing," Ruvolo asserts.

The company is touting the move as further transparency from the brand that first introduced US consumers to commercial sun-care products in the 1940s and went on to set the standard for SPF labeling.