REGULATORY UPDATE
China Expects Earlier Start Of National Marketing Authorization Holder System, p. 20

MANUFACTURING QUALITY
FDA's Kopcha Presses Ahead On Quality Metrics Despite Industry Pushback, p. 14

REIMBURSEMENT
Biosimilars Payments In Medicare: CMS Signals Willingness To Change, p. 10

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Single Gateway For EMA-HTA Advice May Answer All Stakeholders' Needs

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The launch of a new single platform by the European Medicines Agency and the EU network of health technology assessment bodies (EUNetHTA) to offer simultaneous, coordinated advice to companies has been welcomed by the European Federation of Pharmaceutical Industries and Associations as it could allow companies to "work on a single global development plan to answer all stakeholders' needs."

The new platform replaces the parallel scientific advice offered by the EMA and health technology assessment (HTA) bodies under a procedure the agency introduced in 2016, following the completion of a successful five-year pilot of the process. Under this procedure, which was discontinued on July 7, drug companies had to contact HTA bodies in the EU member states individually. *(Also see "EU Pilot Shows Single Drug Development Plan Can Meet Both Regulator And HTA Needs" - Pink Sheet, 5 Apr, 2016.)*

Under the new platform, there will be a "single gateway" for companies to request parallel consultations with the EMA and HTA bodies on evidence-generation plans to support decision-making on marketing authorization and health technology assessment.

Specifically, companies will have to simultaneously notify the EMA and EUnetHTA of their plans to seek parallel advice. EUnetHTA's Early Dialogue Secretariat will then coordinate the involvement of the HTA bodies that will take part in the parallel advice, taking into account the preferences of the requester. Companies would be able to request consultations for initial evidence generation and for post-authorization data collection.

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> "EUnetHTA's Early Dialogue Secretariat will coordinate the involvement of the HTA bodies that will take part in the parallel advice, taking into account the preferences of the requester.

EFPIA told the *Pink Sheet* that its members are expecting that the new platform will help guide companies in their development plans. The platform should help companies "deliver one single evidence package for regulatory and HTA purposes," the industry federation said. The joint platform will hopefully be able to address divergences of requests where they exist, it added.

Regarding the now-discontinued parallel scientific advice process and earlier pilots with EUNetHTA, EFPIA said these had helped its members gain experience and "represented extremely positive steps forward," but required "some additional consolidation." For example, improvements were needed in terms of simplification of logistics, co-ordination of HTA bodies both up-front and in issuing follow-up advice, and the involvement of patients. "We expect that the new joint platform will address these issues," the association said.

EFPIA said it supported the single platform as it could result in the EMA's and HTA bodies' clinical requirements to overlap. Also, in the future the initiative could result in an "optimised joint European assessment of relative efficacy at [the] time of

CONTINUED ON PAGE 4

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Trump Lauds Big Pharma Collaboration On Super Strong Glass Packaging

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President announces Merck, Pfizer and Corning collaboration on new glass packaging for injectable drugs as part of "Made In America Week;" says FDA is streamlining regulations.

FDA and Drug Pricing: Lowering The Cost of Capital – Not The Cost Of Drugs

https://pink.pharmamedtechbi.com/PS121156

FDA regulatory reforms have been framed as part of the drug pricing debate. Commissioner Gottlieb has reframed the goal as lowering the cost of capital by increasing predictability. That probably won't lower drug prices – but it might lower the cost of future acquisitions for drug companies.

Sen. Cassidy Suggests Importing Generics From EU To Pressure US Prices

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Idea may require tweaking existing agreements between FDA and EMA, but is another twist on drug importation, a concept that FDA opposes.

Children To Get A Voice In EMA Scientific Discussions

https://pink.pharmamedtechbi.com/PS121148

Patients under the age of 18 will be allowed to take part on a case-by case basis in EMA discussions on the development and assessment of medicines for children and adolescents.

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inside:

CONTINUED FROM COVER

[product] launch to foster convergence in evidence evaluation and… facilitate alignment of data requirements."

PENDING REQUESTS FROM DISCONTINUED PROCESS

The now discontinued parallel scientific advice process drew 23 requests from companies in 2016, while 18 procedures were started in 2017 (as per data from the July meeting of the EMA's Scientific Advice Working Party).

When the process was discontinued, there were seven requests pending from six companies that had not started, and in all these cases the EMA has contacted the applicants asking them to voluntarily switch to the new platform. "Any potential implications are being discussed by EMA and EUnetHTA with the applicant," an EMA spokesperson told the *Pink Sheet*. Companies that do not want their requests for parallel EMA-HTA scientific advice to be treated through the new platform were given a week to notify the agency.

CONSOLIDATED AND INDIVIDUAL PARALLEL CONSULTATIONS

The new single platform, the EMA explained, offers several advantages over the earlier process, such as: centralized recruitment of HTA bodies taking into account the company's preferences; increased mutual understanding and the ability to solve problems through a more structured interaction between EMA the and HTA bodies; and streamlined logistics for companies requesting advice.

The new platform was launched under EUNetHTA's Joint Action 3, Work Package 5 (WP5), which deals with a life cycle approach to improve evidence generation. It has a big outreach with nearly 40 of the 81 partners within EUnetHTA's Joint Action 3 being involved in the activities of WP5, the EMA explained. WP5 has France's Haute Autorité de Santé (HAS) as lead partner and Germany's Gemeinsamer Bundesausschuss (G-BA) as the co-lead partner.

The experience of HAS and G-BA – along with the participation of the newly established Early Dialogues Working Party that is composed of HTA bodies from France, Germany, the UK, Italy, Hungary and the shared seat of the Netherlands and Belgium – will help to ensure that EUnetHTA's contribution to evidence generation activities, including those of the parallel consultation platform with the EMA, "is of high-quality and reflects the breadth of perspectives within EUnetHTA," the EMA spokesperson said.

Under the new platform, with respect to scientific advice from HTA bodies, there are two different pathways for parallel consultation – consolidated or individual; the difference between the two is the mode of participation of the HTA bodies. Under consolidated parallel consultations, all EDWP members would participate in the procedure as well as up to three additional HTA bodies, forming the so-called Early Dialogue Committee (EDC).

In individual parallel consultations, HTA bodies will be recruited to participate in an early dialogue on a voluntary basis based on their national-level priorities and availability. "In both pathways, preferences of the applicant will be taken into account, but participation of those HTA bodies is not guaranteed," the EMA said.

The recruitment of HTA bodies for the individual and consolidated parallel consultation process will be handled by the EUnetHTA Early Dialogues Secretariat. Under both processes, a scientific coordinator will be assigned to the procedure to:

- facilitate discussion between HTA bodies in advance of meetings;
- prepare a consolidated list of issues and comments from participating HTA bodies;
- interact with the EMA; and
- act as a co-chair for the HTA bodies for the face-to-face meeting.

The final output from individual parallel consultations will be in the form of individual written reports from the participating HTA bodies. For consolidated parallel consultations, an HTA rapporteur(s) will be assigned to collect and consolidate responses from the EDC and present consolidated HTA answers during the face-to-face meeting.

Due to resource constraints under EUNetHTA Joint Action 3, the EMA explained that it would only be possible to select "a limited number of medicines" for consolidated parallel consultations. For this process, the EDWP would select medicines that aim to bring added benefit to patients.

PROVIDING CHMP ASSESSMENT REPORTS TO EUNETHTA

Separately, progress is also being made on another initiative under which the EMA's human drugs evaluation committee, the CHMP, plans to provide its assessment reports to EUNetHTA when it delivers an opinion on whether a drug should be authorized. Under this initiative, EUnetHTA will identify products that fall in the scope of joint relative effectiveness assessment (REA) production under EUnetHTA Joint Action 3, Work Package 4 (WP4), and will notify the EMA. At present, two products have been notified and work is ongoing, the EMA said.

Under this initiative, only elements of the final CHMP assessment report that are relevant to HTA will be shared. "These are generally the sections concerning introduction/problem statement, clinical aspects (efficacy/safety), benefit-risk balance and recommendations," the spokesperson said.

Once a product is selected, a joint communication from the EMA and EUnetHTA is sent to the concerned company with details on the elements to be shared. This information is shared under confidentiality arrangements once the final CHMP assessment report has been adopted and once the applicant has received the final assessment report with the opinion package, the EMA explained.

During the development of this initiative, industry representatives had welcomed the collaboration, which promises to facilitate mutual understanding of decision making.

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You Say Goodbye, I Say Hello – MHRA Moves In, EMA Moves Out

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The MHRA is set to move to Canary Wharf next year.

The UK Medicines and Healthcare products Regulatory Agency is on course to move next year to Canary Wharf, the east London financial district that the European Medicines Agency currently calls home but is being forced to leave as a result of the UK's decision last June to leave the EU.

The MHRA is due to move from its central London location of Victoria to a new government hub in Canary Wharf in the first half of 2018, according to the agency's newly published 2016/17 annual report. It is not known yet when, or to where, the EMA will move.

The move appears to be part of a big government cost-cutting initiative that involves moving thousands of civil servants to a modern government hub in Canary Wharf.

The MHRA comprises three centers – the MHRA regulator, the Clinical Practice Research Datalink and the National Institute for Biological Standards and Control – and, according to its latest annual report, it employed around 1,257 permanent full-time equivalent staff last year.

The report notes the move could lead to the loss of key staff "if they perceive they are moving to a less accessible location with inadequate space and facilities, which would cause disruption to the agency's operations." The MHRA says it is planning to develop "appropriate measures" to mitigate the impact on staff. Its relocation

The six criteria for hosting the EMA, as endorsed by the European Council

The assurance that the agency can be set up on site and take up its functions at the date of the UK's withdrawal from the EU. This criterion concerns in particular the availability of appropriate office space. This should include the necessary logistics and sufficient space for offices, meeting rooms and off-site archiving, high-performing telecommunication and data storage networks as well as appropriate physical and IT security standards.

The accessibility of the location. This criterion concerns the availability, frequency and duration of flight connections from the capitals of all EU member states to the airports close to the location, the availability, frequency and duration of public transportation connections from these airports to the location, as well as the quality and quantity of accommodation facilities. In particular, the criterion implies the capacity to allow for the continuation of the volume and intensity of current meeting activities of the agency.

The existence of adequate education facilities for the children of agency staff. This criterion concerns the availability of multi-lingual, European-oriented schooling that can meet the needs of the children of current staff as well as the capacity to meet future education needs.

Appropriate access to the labor market, social security and medical care for both children and spouses. This criterion concerns the capacity to meet the needs of the children and spouses of current as well as future staff for social security and medical care, as well as the availability of job opportunities for them.

Business continuity. This criterion is relevant given the critical nature of the services provided by the agencies and the need to ensure continued functionality at the existing high level. It relates to the timeframe required to fulfil the four criteria above. It concerns among other things the ability to allow the agencies to maintain and attract highly qualified staff from the relevant sectors, notably in case not all current staff should choose to relocate. It also concerns the capacity to ensure a smooth transition to the new location and to guarantee the business continuity of the agencies.

Geographical spread. This relates to the agreed desirability of geographical spread of the agencies' seats, and to the objective set in December 2003 by the representatives of the member states.

> "There is currently no evidence to suggest staff are leaving the agency as result of the planned move" – MHRA

team will develop an internal communications program to keep staff informed.

An MHRA spokesperson told the *Pink Sheet* that "with the move not expected to happen before mid-next year, there is currently no evidence to suggest staff are leaving the agency as result of the planned move." The spokesperson added that the agency was pleased to have secured modern new accommodation and that it was "currently seeking feedback from staff on how they may be impacted by the move for consideration by the move project team."

An "Accommodation Needs and Vision Project" group has produced a report setting out the agreed "vision" for the agency's future accommodation and requirements for the move, according to the annual report. This involves having work environments that will be "inspiring and productive, supported by reliable and effective technology, enabling us to choose flexible work-styles," the MHRA said. "This will enable us to deliver the Agency's mission, encourage a more inclusive, collaborative and professional culture, and provide the best service to our stakeholders and customers."

UGLY, FRAGMENTED OFFICES

The government first announced it would be moving 5,700 full time civil and public servants from their offices in central London to east of the city in December last year. The move, which is due for completion by the end of 2018, is part of a drive to modernize the civil service. "Relocating civil and public servants from existing, often fragmented office locations, to modern, cross-departmental workplaces will make the most of emerging working practices and technology is part of that drive," the government said. The new hub in Canary Wharf would provide "a better working environment for many London-based Civil Servants at considerably less cost to the taxpayer." The approach will be replicated across the UK, "putting right the historic mistake of forcing public servants to work in ugly and expensive buildings."

GERMANY WANTS BONN TO HAVE EMA

EU member states wanting to house the EMA post-Brexit – the UK is due to leave the EU at the end of March 2019 – must submit their bids by the end of July. A decision on the new location of the agency is expected in November. *(Also see "EU Postpones Decision On EMA's New Home To November" - Pink Sheet, 23 Jun, 2017.)* Perhaps then there will also be some clarity around the timing of its departure from London.

Germany is joining the ranks of those bidding to host the EMA, which currently employs almost 900 people. Germany would house the agency in Bonn. Many countries are competing for the agency in addition to Germany, including Sweden, Denmark, Ireland, France and Spain. The official website for the Bonn candidacy is www.closer-to-europe.eu.

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REGULATORY UPDATE

Drug Pricing: Could Expedited Review Of Competing Brands Create The Desired Pressure?

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Priority review of innovator products, a valuable tool for brand drug development, also may be able to help FDA fight the drug pricing problem.

Usually it is the brand industry that is considered at least partially responsible for the problem of rising drug prices, which is why the agency held a public meeting July 18 on the Hatch-Waxman Act and whether agency regulation of the generic industry needed tweaking.

But some payer groups argued that FDA could create more competition and pricing pressure using the new drug approval process instead of just the generic drug pathway.

Paul Eiting, senior manager of value-based policy for Blue Cross Blue Shield Association, told the FDA panel at the meeting that prioritizing review of brand products in markets with little or no competition could affect prices.

"The FDA drug application review process could be improved to prioritize branded products where there are no competitors in a therapeutic class," he said.

Eiting compared the idea to FDA's announcement in late June that it would prioritize generic applications for reference products with fewer than three approved ANDAs. *(Also see "FDA Drug Pricing Policy Offers Short-Term PR Gain, More Long-Term Actual Benefit" - Pink Sheet, 27 Jun, 2017.)*

Eiting said Blue Cross/Blue Shield's idea focused on product classes, not indications, where there are no competitors. He said granting priority review to the others undergoing FDA review about the same time or even a year later would allow them on the market sooner.

"Especially in cases where you have a first-in-class drug … and then you would have manufacturers catching up to try to enter the market in the same molecular class," Eiting said.

The suggestion was a substantial divergence from most of the meeting's themes, many of which centered on problems with the brand industry and solutions targeted to help generic sponsors. Many speakers asked FDA to deal with product evergreening, delays created by citizen petitions, and abuses of the Risk Evaluation and Mitigation Strategy (REMS) system.

FDA Commissioner Scott Gottlieb also said the agency would consider publicizing the letters it writes to brand companies indicating they could sell samples to generic companies without violating the REMS in the hopes of curbing the abuse.

AN INDUSTRY DILEMMA

Expediting brand competitors for first-in-class products presents an interesting conundrum for the brand industry. While sponsors likely would embrace another opening for expedited approval and a faster route to market, they may cringe at the idea that innovative products are a fundamental part of the pricing problem.

Blockbuster therapies and the treasure chest they bring for companies can help fund future drug development. Cutting into that potential also may limit companies' activities.

Other incentives also could be affected, such as the priority review voucher system. The value of the coupon guaranteeing an expedited review may drop further if Eiting's idea is implemented. *(Also see "Priority Review Vouchers Appear To Be Dropping In Price" - Pink Sheet, 27 Jul, 2016.)*

HEP C MARKET A PRIME EXAMPLE

Prioritizing brand products, seemingly by allowing them priority review, would be rooted in unmet patient need.

Marissa Schlaifer, a consultant pharmacist representing the Pharmaceutical Care Management Association, said during the meeting that FDA could include unaffordability as part of the unmet need when considering an application, which could spur a treatment gaining access to the pathway.

"We believe unmet medical needs should encompass lack of access when brand products are priced high and face no or little competition," Schlaifer said. "If the price of a drug is so high that a patient who needs it cannot afford it, a concept some call financial toxicity, the patient's medical needs is still not met."

"We believe unmet medical needs should encompass lack of access when brand products are priced high and face no or little competition."
– Marissa Schlaifer, Pharmaceutical Care Management Association

Schlaifer argued that data suggests creating more head-to-head competition in a therapeutic class, even with additional brand products, can lower prices.

The Hepatitis C market is one example, she said.

Gilead Sciences Inc. dominated when *Sovaldi* (sofosbuvir) was approved in December 2013 and *Harvoni* (sofosbuvir/ledipasvir) was approved in October 2014.

But soon after Harvoni's approval, FDA began clearing competitors. **AbbVie Inc.**'s *Viekira Pak* (ombitasvir/paritaprevir/ritonavir) was approved in December 2014, and followed by several others. *(Also see "INFOGRAPHIC: Hepatitis C Market Still Has Room To Grow" - Scrip, 1 Aug, 2016.)*

Viekira Pak received a priority review and was designated a breakthrough therapy. Schlaifer said a second entrant into the market led to nearly 50% price concessions, which opened treatment to more patients.

"As costs fell, health plans offered the drug to substantially greater populations of patients, thus meeting existing medical needs that had previously been unmet," she said.

Once other Hep C treatments began entering the market, Gilead saw therapy starts drop, even as revenue remained high. *(Also see "Gilead Faces Challenges In HCV, But Competitors Would Switch Places" - Scrip, 12 Feb, 2016.)*

Gilead came back with another sofosbuvir combination product for Hep C, *Vosevi* (sofosbuvir/velpatasvir/voxilaprevir), which FDA approved July 18. *(Also see "Gilead Completes HCV Clinical Development With Vosevi Approval" - Scrip, 18 Jul, 2017.)*

BUT EXPEDITING APPLICATIONS, MEANS LESS RESOURCES FOR STANDARD REVIEW

At the same time, one analyst warned FDA that devoting more resources to expediting brand reviews likely would not be possible without a price.

Alex Brill, CEO of Matrix Global Advisors, who has conducted several analyses on behalf of the Association for Accessible Medicines, said during the meeting that brand products can compete on price, although not always, and additional emphasis on expedited pathways for new drugs may lead to less focus on other applications.

"Unmet needs is an appropriate, reasonable area for which the agency should be working diligently and is, but it comes at that

cost," he said.

Brill added that FDA needs additional resources or should be aware that focusing on expedited pathways comes at the expense of standard review.

FDA and others are hoping priority review of generics in particular can create more competition and push prices down. The FDA Reauthorization Act, which has passed the House and is pending in the Senate, includes incentives for some generic approvals. *(Also see "User Fee Bill Or Drug Pricing Bill? House Members Makes Both Cases" - Pink Sheet, 12 Jul, 2017.)*

The bill also would renew the generic drug user fee program and create an ANDA priority review pathway. *(Also see "ANDAs Can Get Priority, Eight-Month Reviews Under User Fee Deal" - Pink Sheet, 24 Sep, 2016.)*

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FDA Exploring Whether Public Shaming Can Stop REMS Abuses

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The US FDA may resort to using its bully pulpit to lessen REMS abuses that prevent generic entry.

Agency letters to brand companies indicating it is acceptable under a Risk Evaluation and Mitigation Strategy (REMS) to sell samples to a generic company for testing may be made public, Commissioner Scott Gottlieb said during the July 18 public meeting on ensuring the Hatch-Waxman Act continues to balance access and innovation.

FDA called the meeting to explore whether changes to generic laws and policy are needed amid problems with rising drug prices.

Generic firms have long complained that brand companies with products covered by a REMS often refuse to allow them to purchase product for sampling because it would violate aspects of the plan.

In 2014 draft guidance, FDA said it would officially notify a brand company in writing that it was not a REMS violation to allow the sale to the generic company. *(Also see "Generics REMS Hurdles Lowered Somewhat By FDA Protocol Letters" - Pink Sheet, 4 Dec, 2014.)*

The program has not met with widespread success. Gottlieb told meeting attendees that the agency is reviewing the guidance and "actively considering whether it achieves its goals."

REMS letters to brand companies could be released "to make more widely known the instances where generic drug makers may be having trouble getting access to branded drugs," Gottlieb said.

Whether releasing the letters would break the log-jams is unclear. The hope seems to be that disclosure (and the resulting public pressure) may help generic sponsors gain access to the products and potentially curb abusive practices.

FDA called the meeting to explore whether changes to generic laws and policy are needed amid problems with rising drug prices.

"These letters could contain important information that can help inform broader discussions about access and competition," Gottlieb said. "Their public release could be one step to help ensure that unnecessary hurdles to generic drug development are removed."

FDA did not offer a timeline for when a decision on publicizing the letters will be made.

The idea follows on Gottlieb's interest in agency transparency. He also has suggested releasing complete response letters, in part because they could help inform the public about FDA's review process. *(Also see "Gottlieb Q&A: Confirmation Is Nearing, Will Complete Response Letters Finally Get Released?" - Pink Sheet, 5 May, 2017.)*

What has become known as REMS abuse is not a new problem, but finding a solution to it has been a challenge for the generic industry. In 2012, an early draft of the FDA Safety and Innovation Act included a REMS

abuse provision, but it was removed after lobbying by the brand industry. *(Also see "REMS Abuse Legislation: GPhA and PhRMA Set To Battle Again" - Pink Sheet, 15 Jun, 2016.)*

A representative of the Pharmaceutical Research and Manufacturers of America (PhRMA) did not offer an opinion of the idea when asked by FDA officials at the meeting.

In a later presentation, PhRMA suggested that REMS abuse was not a serious problem in need of reform because there are some generics that have come to market with a REMS. Publicizing the agency's letters could deflate that argument by highlighting instances where generics have not been able to come to market, but the policy shift probably won't dent another industry argument against REMS reforms – providing large quantities of samples is a burden for small firms.

REMS letters could become part of the agency's Drug Competition Action Plan, intended to use agency resources to increase competition and potentially help bring down drug prices.

FDA announced in June that the plan also included a change to internal policy to prioritize ANDAs for reference products where there are fewer than three approved applications. *(Also see "FDA Drug Pricing Policy Offers Short-Term PR Gain, More Long-Term Actual Benefit" - Pink Sheet, 27 Jun, 2017.)*

FDA ALSO A PROBLEM WITH REMS LETTERS

Not surprisingly, many stakeholders raised the problem of REMS being used to prevent generic entry during the meeting.

Michael Carrier, distinguished professor at Rutgers Law School, agreed that the letters should be made public, in part because brand companies sometimes simply ignore them.

But FDA also was implicated as a potential barrier. Candis Edwards, senior VP of clinical regulatory affairs at **Amneal Pharmaceuticals LLC**, said the company has submitted seven requests for REMS letters since 2015.

REMS letters could become part of the agency's Drug Competition Action Plan, intended to use agency resources to increase competition and potentially help bring down drug prices.

Edwards said on average the agency review to determine whether a letter is warranted has taken 18 months. She said FDA has sent two letters sponsors, and of those requests, one was resulted in receiving product.

Edwards asked that the agency commit to a formal review timeline for the reviews, suggesting three to six months.

SUBMISSION GUIDANCE, ANDA ASSESSMENT PRACTICES BEING DEVELOPED

FDA also intends to update to its internal policy on ANDA review again, as well as offer industry more guidance on the submission practices.

Gottlieb said that a Manual of Policies and Procedures document on Good ANDA Assessment Practices will be released outlining how the agency can streamline the review process, including eliminating duplicative procedures.

The MaPP will include several new changes to the ANDA review process.

Primary ANDA assessments should focus on "need-to-know" regulatory requirements. Gottlieb also said practice will change such that supervisors will validate, rather than re-do the assessment, and their scrutiny will "vary according to the experience level of the primary reviewer and risk and complexity of the product." If a complete response letter is required, it should "clearly state what needs to be fixed" and if it is not clear, the reviewer should follow-up and explain the issues over the phone, he said.

Gottlieb indicated that GDUFA II review goals will not change because "truncating [the] review prevents applicants from fixing their submissions and getting them approved."

At the same time, FDA also is preparing guidance for sponsors on Good ANDA Submission Practices that should include many familiar items. Gottlieb said it will state "common, recurring deficiencies that we see in applications and provide advice on how these problems can be avoided."

Both documents are expected by the end of the year and intended to help cut the number of ANDA review cycles. Many now require three or more cycles before approval. FDA would prefer the average be one or two. *(Also see "ANDA Reviews: First-Cycle Desired, But Two-Cycles OK?" - Pink Sheet, 27 Jul, 2015.)*

FDA has argued that submission quality also must improve. *(Also see "Generic Drugs: First-Cycle Review Times Improve, But Hundreds Of ANDAs Still Pending" - Pink Sheet, 4 Jul, 2017.)*

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Biosimilars Payments In Medicare: CMS Signals Willingness To Change

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The Centers for Medicare and Medicaid Services is re-thinking its Medicare Part B policy for reimbursing biosimilars and is seeking public comments on how it might revise its approach.

"Although we believe that the United States biosimilar biological product marketplace is still in an early phase (because only a few products are on the market), we are interested in assessing the effects of Medicare payment policy on this important portion of the Part B drug marketplace at this time, particularly for fostering a robust and competitive marketplace and encouraging the innovation that is necessary to bring these products to the marketplace," CMS said in the 2018 Medicare Physician Fee Schedule proposed rule, released July 13.

> *"It is CMS's goal to further investigate a solution that allows market forces to provide a robust and comprehensive selection of choices for patients as a fair price," the proposal states. "It is essential to take a measured approach that considers all options."*

The current approach calls for biosimilars referencing the same drug to be reimbursed by Medicare under the same Healthcare Common Procedure Coding System (HCPCS) code, which would result in one weighted average sales price for all products within a shared code. CMS still plans to assign individual codes to innovator drugs, which would set a payment rate that is separate from the biosimilars.

The policy relates only to biosimilars covered under Part B, which are those administered by a physician or other health care provider. It was announced in the fall of 2015 and became effective Jan. 1, 2016. *(Also see "CMS Sticks With Combining Biosimilars In Single Medicare Payment Code" - Pink Sheet, 30 Oct, 2015.)*

The prospect that things may change is welcome news for biosimilar developers, health care providers and other stakeholders, who have argued the policy would undercut innovation and competition and urged that instead, CMS should establish individual reimbursement codes for each product.

The Biosimilars Forum, which represents product developers, said July 13 it is "pleased that CMS values additional thought and analysis of this important issue," and pledged to "continue to work with other stakeholders and CMS to provide additional comment and guidance regarding this reimbursement issue during the open rulemaking process." Comments on the proposal are due Sept. 11.

"It is CMS's goal to further investigate a solution that allows market forces to provide a robust and comprehensive selection of choices for patients as a fair price," the proposal states.

The impact of the current policy has not yet been tested in the market because the only two biosimilars that have launched, **Sandoz Inc.**'s *Zarxio* (filgrastim-sndz) and **Celltrion Inc.**'s *Inflectra* (infliximab-dyyb), reference different innovator drugs.

CURRENT POLICY WOULD BE TESTED IN COMING MONTHS

However, it may be put into practice in the coming months, unless CMS reverses it. **Merck & Co. Inc.** is expected to introduce a second infliximab biosimilar, *Renflexis*, by the fall, after gaining approval in April. *(Also see "Samsung's Renflexis: Second US Biosimilar To Janssen's Remicade, With A Few Firsts" - Pink Sheet, 21 Apr, 2017.)* Because Inflectra and Renflexis both reference **Janssen Pharmaceutical Cos.**' *Remicade*, they would get the same Medicare payment rate, under the existing approach.

Other examples are on the horizon.**Apotex Inc.** is developing another filgrastim biosimilar that would compete with Zarxio, both referencing **Amgen Inc.**'s *Neupogen*. And at least four biosimilars in development reference Amgen's *Neulasta* (pegfilgrastim) and two reference **AbbVie Inc.**'s *Humira* (adlimumab). *(Also see "US Biosimilars: 40% First-Cycle Approval Rate Leaves Room For Improvement" - Pink Sheet, 6 Jul, 2017.)*

CMS expressed interest in suggestions on how to handle reimbursement for biosimilars with fewer approved indications than their reference drug or "situations where different biosimilars may be licensed for different subsets of indications for which the reference product is licensed."

The agency adds, "we are particularly interested in obtaining material, such as market analyses or research articles, that provide data and insight into the current economics of the biosimilar market place. This includes patient, plan and manufacturer data both domestic and, where applicable, from European markets that may be more established than, and provide insight for, the current Unit-

Shutterstock: David Crocket

ed States market."

Data demonstrating how individual HCPCS codes could impact the market would be helpful, CMS says, including the impact on "innovation, the number of biosimilar products introduced to the market, patient access, and drug spending."

The agency is additionally interested in comments on Medicare Part B reimbursement in the broader biologics market. "We also seek comment regarding other novel payment policies that would foster competition, increase access, and drive cost savings in the biological product marketplace," according to the proposal. "These solutions may include legislation, demonstrations, and administrative options."

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340B REFORMS: Oversight Hearing Suggests Slow, Piecemeal Approach

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The House Energy & Commerce/ Oversight Subcommittee's July 18 hearing on the 340B drug discount program suggests that there is serious, bipartisan interest in updating the 1992 legislation that created the program – but that the process will move forward slowly and carefully.

Subcommittee Chairman Tim Murphy (R-Pa.) and Ranking Democrat Diana DeGette (D-Colo.) gave every indication of intending to continue their review of the program, with a focus on identifying specific, discrete changes that could help better assure that the discount is being used appropriately.

Full committee chairman Greg Walden (R-Ore.) explicitly framed the hearing as part of a long-term, ongoing effort. "The committee has been reviewing the Health Resource & Services Administration's oversight of the 340B drug pricing program for over two years, and plans to continue this work after the hearing," he said.

Walden also captured the note of caution that resonated throughout the hearing: there is bipartisan support for the core goal of the 340B program in supporting safety net providers: "As we move forward, it's also important not to overreact and create unnecessary red tape for providers who are truly using the program to benefit patients."

In the context of a generally partisan climate for health care legislation – and especially in the midst of at times heated

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> "As we move forward, it's also important not to overreact and create unnecessary red tape for providers who are truly using the program to benefit patients." – Chairman Walden

debates between pharmaceutical manufacturers and 340B purchasers about the realities of the discount program – the tone of the hearing was noteworthy.

There was a partisan divide: Republicans on the committee tended to emphasize the need-for-more-oversight theme, while Democrats tended to emphasize the "don't-overreact" theme. But there seemed to be a shared interest in assuring that HRSA has the tools it needs to run the program.

RESTORING REGULATORY AUTHORITY AS A FIRST STEP?

That focus on understanding technical aspects of program operations and oversights will potentially be time-consuming and argues against near-term legislation. However, there may be a push for a very straightforward change to restore HRSA's authority to issue implementing regulations for the program.

HRSA's efforts to spell out program definitions were disrupted by a court ruling in 2014 that held that the agency has no authority to issue regulations under the 340B statute, except in narrow circumstances stipulated in the 2010 Affordable Care Act.

The next step is likely to be a hearing that includes hospitals and other purchasers testifying about the impact of the savings on their ability to provide care.

That message was reinforced by the three witnesses: HRSA Office of Pharmacy Affairs Director Krista Pedley, Government Accountability Office Health Care Director Debra Draper, and HHS Assistant Inspector General Erin Bliss.

The next step is likely to be a hearing that includes hospitals and other purchasers testifying about the impact of the savings on their ability to provide care. There were no specific mentions of next steps or upcoming hearings. However, Murphy and DeGette both suggested further questions and topics for exploration, and spoke directly to each other about areas for further clarification.

Murphy specifically thanked HRSA for providing information about its recent audits of covered entities as requested by the committee last month, and promised to follow up with more specific questions after reviewing the material.

DeGette noted in the opening questions for the panel of witnesses that there seemed to be a lot of interest in better understanding how hospitals account for and use the savings from the 340B discount. Those questions are "appropriate," she said, but "we don't have anyone here who can answer that question."

"Maybe we should have a follow up hearing and have someone from the hospitals come and talk about what they do with that money," DeGette said.

Rep. Chris Collins (R-N.Y.), one of the most vocal critics of the 340B program in Congress, used his question time to push the idea that re-establishing clear regulatory authority for HRSA "could be a very quick starting point" for legislation. "What do you need from us?" he asked Pedley. "Guidance is guidance. Do you need more regulatory authority from Congress or don't you?"

Pedley noted that the Trump Administration's proposed 2018 budget includes a call for established broad regulatory authority for the 340B program. Collins asked if there was formal legislative language drafted by HRSA for the committee to consider, saying "I would think fairly quickly we could move that through."

Collins' willingness to discuss a standalone fix to HRSA's regulatory authority – rather than more comprehensive changes he is drafting in a separate bill – is in part an acknowledgement that enacting substantive legislation remains a challenge.

However, it is also likely a reflection of his expectation that the current Administration would use its regulatory authority to accomplish many of the goals of his legislation. *(Also see "340B Reform May Return To Capitol Hill: Hearings Will Play To New HRSA Leadership" - Pink Sheet, 4 May, 2017.)*

One of the program's vocal defenders, Florida Democrat Kathy Castor, on the other hand, indicated wariness about providing stronger regulatory authorities. "I strongly favor appropriate HRSA oversight to assure program integrity." However, she noted concerns with HRSA's proposed guidance (since withdrawn) that would have curbed use of the discount in settings like discharge prescriptions and infusion services. "If we give you authority, how should we be assured that harmful proposals such as these wouldn't go beyond the Congressional intent?" Castor asked.

The Democratic minority leadership on the committee spoke out against the Trump Administration's proposal to cut Part B payments for 340B-priced drugs used by hospital outpatient departments. *(Also see "Closing The Spread: 340B Providers Face Sharp Cuts Under Medicare Proposal" - Pink Sheet, 17 Jul, 2017.)*

DeGette said she was "troubled" by that rule – and especially by the claim that it would address the costs of prescription drugs. "That statement seems more fantasy than reality. The proposed rule will do nothing to achieve the goal of making prescription drugs more affordable to the general population," she said. "It tries to solve one problem by creating many others" and "threatens to undermine the important safety net mission of 340 hospitals."

Full committee ranking Democrat Frank Pallone (N.J.) made comments, and joined DeGette in urging the E&C Committee to look directly at drug pricing. "I am always happy to have a conversation to strengthen the 340B program," Pallone said. But "it would be disingenuous for anyone to say this hearing is about rising drug prices."

Republicans were notably silent on the proposed Part B payment cuts, though Collins and Rep. Buddy Carter (R-Ga.) did speak up to support the argument that 340B discounts do lead to higher costs elsewhere in the system. "There is no free lunch in America," Collins declared. If 340B hospitals are buying high-priced oncology drugs at a discount, "the price of the drugs goes up" for other purchasers.

From the editors of the RPM Report.
Published online July 18, 2017

Can The FDA Climate Be Too Good?

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Amicus Therapeutics had some surprising good news on July 11: it will be submitting an NDA for its potential Fabry disease therapy migalastat in the fourth quarter, rather than needing to run a new Phase III study to support a filing.

The news came just eight months after Amicus announced that it would *not* be able to file based on existing data, because FDA told the company that it would not consider an accelerated approval based on kidney globotriaosylceramide (GL-3) measurements. That sounded like a final decision, and Amicus' investors – at least – were expecting the next update to be the launch of a study measuring GI endpoints.

Instead, Amicus said that "based on a series of discussions with and written communication received from the FDA," it has the greenlight to file for Accelerated Approval based on "existing data, including reduction in disease-causing substrate (GL-3), as well as the totality of data from completed clinical studies." *(Also see "FDA Reversal Gives Amicus Renewed Hope For US Oral Fabry Launch" - Pink Sheet, 11 Jul, 2017.)*

The news was surprising – but also very much in keeping with the current climate of extreme flexibility at FDA, especially for rare disease therapies. But this case has special resonance, thanks to the very public role played by Amicus CEO John Crowley and his daughter Megan in supporting the Trump Administration's call for greater regulatory flexibility at FDA.

Megan Crowley, a Pompe disease patient, was a guest at Trump's first address to Congress in February. After introducing her, Trump criticized FDA. "Our slow and burdensome approval process at the Food and Drug Administration keeps too many advances, like the one that saved Megan's life, from reaching those in need," he said. "If we slash the restraints, not just at the FDA but across our government, then we will be blessed with far more miracles like Megan."

The news was surprising – but also very much in keeping with the current climate of extreme flexibility at FDA, especially for rare disease therapies. But this case has special resonance.

(Also see "Trump Slams FDA Regulations In Joint Session Of Congress" - Pink Sheet, 28 Feb, 2017.)

While it seemed somewhat odd to point to a patient who benefited from an FDA approved medicine to criticize the agency, it wasn't too hard to connect the dots between Trump's comments and Amicus' recent setback at FDA – particularly since John Crowley met with Trump before the address.

That begs the question of whether FDA's new flexibility in this case is a reflection of carefully scientific review, or a product of political interference.

Amicus, of course, sees it as the former: the company notes that it submitted new safety analyses and also provided updated post-marketing experience from Europe. And there is no question that FDA is looking carefully at all rare disease therapies to find ways to ease the pre-market data collection in response to patient need.

However, just as Trump relied on a caricatured picture of FDA in his Congressional address, critics of the FDA will find it very easy to paint the decision to accept the filing as a politically motivated act – and it is impossible for FDA to prove that it wasn't affected by the extremely high profile Presidential attention to the issue.

Whether Trump's relationship with Crowley had anything to do with FDA's change of heart is ultimately beside the point. If migalastat is approved and then something goes awry, there will be plenty of people ready to say FDA abandoned its standards under political duress.

The history of FDA is filled with pendulum swings, and one sure way to encourage a swing back towards caution and inflexibility is to have the public start to question the independence and scientific basis for FDA's actions. That is why the good news for Amicus may end up being bad news for innovators in the long run.

From the editors of the RPM Report. Published online July 17, 2017

FDA's Kopcha Presses Ahead On Quality Metrics Despite Industry Pushback

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"We can't just turn it into a gripe session where people say, 'FDA does this, this and this, we don't like this, this and this. It's like OK, well then, what is it you do like? What are some potential solutions?"

The frustrating juncture that US FDA's quality metrics initiative has reached was evident at a recent quality manufacturing conference hosted in Arlington, Va., by the International Society for Pharmaceutical Engineering, FDA and the Pharmaceutical Quality Research Institute.

At the outset of the ISPE quality meeting, Michael Kopcha, director of FDA's Office of Pharmaceutical Quality and an honorary conference chair, rebuked the largely industry audience for fighting the initiative instead of trying to help make it work.

"We can't just turn it into a gripe session where people say, 'FDA does this, this and this, we don't like this, this and this. It's like OK, well then, what is it you do like? What are some potential solutions?"

Later in conference workshop sessions, participants responded with some creative ideas. The only problem was they were evenly divided between supporting FDA's basic approach to quality metrics and switching to a more complex type of scheme that would be more comfortable for industry but rather useless for FDA.

Meanwhile, firms wanting to participate in the initial voluntary phase of the quality metrics initiative are worried whether they will have enough time to prepare.

It will take some work to establish metrics reporting systems that conform to whatever scheme the agency pilots, and the scheduled January 2018 launch of the voluntary phase is fast approaching.

HOW THE CONFLICT OVER QUALITY METRICS BREWED

FDA's Nov. 25 revised draft guidance resolved issues industry had raised about the initial July 2015 draft and established an implementation approach that begins with a voluntary phase outlined in the guidance and advances to a mandatory phase that would be established by rule. *(Also see "FDA's Revised Quality Metrics Program: Voluntary Now, Mandatory Later" - Pink Sheet, 27 Nov, 2016.)*

In February, FDA officials encouraged attendees of a Parenteral Drug Association meeting on quality metrics and quality culture to join the voluntary phase, saying they want broad participation from all industry sectors, not just "the A-plus students." *(Also see "FDA Urges Full Participation In Quality Metrics Program" - Pink Sheet, 24 Feb, 2017.)*

In March, groups representing all sectors of the industry rejected the quality metrics initiative, with the generics sector out front, asserting that it would cost the pharmaceutical industry $1bn per year to comply and urging the White House Office of Management and Budget to scuttle it. *(Also see "US FDA And OMB Should 'Pause' Billion-Dollar Quality Metrics Program, Industry Groups Say" - Pink Sheet, 29 Mar, 2017.)*

Pharmaceutical industry recommendations that made it into White House briefing materials leaked last month included a call to put FDA's quality metrics initiative on hold to allow for further dialogue with industry. *(Also see "White House Mulls Proposal To Pause FDA's Quality Metrics Initiative" - Pink Sheet, 22 Jun, 2017.)*

FDA WANTED FEEDBACK NOT PUSHBACK

In his remarks to the ISPE quality meeting, Kopcha noted that the agency has received "significant pushback from industry. … I'm sure most of you have contributed to that."

However, despite what he said was a record number of comments, "there was really not much where people offered up suggestions."

Kopcha said that "I really was hoping is that we would get some constructive feedback that would help us move quality metrics forward. We didn't really get what we

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had hoped for. It's OK. We're going to still deal with it anyway."

He went on to remind the audience that FDA needs to surveil the industry, identify quality-related trends and press for mitigation where needed to prevent drug shortages.

"I know a number of individuals have looked at quality metrics and been concerned that we're trying to figure out where we can maybe write more 483s or figure out if there's some nefarious things going on behind the scenes. But really it's for us to drive better quality in the pharmaceutical industry."

Quality metrics is one of two activities on OPQ's plate that Kopcha would most like to accomplish, he said in response to a question. The other is the new inspection protocol program.

However, Kopcha also acknowledged that the new commissioner, Scott Gottlieb, has another priority that will take precedence – expediting generic drug reviews.

REPORTERS' LIST GOING AWAY

Steve Greer, external engagement leader in corporate quality assurance at Procter & Gamble, shared the quality metrics workgroup's key findings on the final day of the conference.

Greer serves on the core team for ISPE's quality metrics initiative and helped facilitate workshop discussions on the topic at the meeting.

At the outset, he said FDA's plan to publish a tiered "reporters list" of companies that take part in the initial voluntary phase of the initiative is either going to change or go away, something he said has been acknowledged byTara Gooen Bizjak, a senior science policy advisor at FDA who plays a key role in the agency's quality metrics initiative.

"It just doesn't work as intended, which is to try to encourage and incentivize firms," Greer said. "That's not working well, and we need to figure out a different strategy for that."

WHAT'S ON THE METRICS MENU?

Greer said the workgroup discussed outstanding issues with important quality metrics. They agreed that:

FDA's Kopcha wants constructive feedback

- Quality culture and key behavior indicators are important, but it will take more work to come up with good metrics in this area.
- Despite lots of talk about process capability, no one was ready to commit to a specific metric in this area.
- Recurring deviation rate is a popular metric, except that it is difficult to agree on what constitutes recurring.
- Supplier reliability is another promising area for metrics that will take more work.

One novel idea that surfaced in the discussions was for FDA to offer a menu of metrics to choose from, "as opposed to having three that apply to everyone," Greer said. "This way you could tailor a program to your own particular situation and really drive value there."

DEFINITIONS RESIST STANDARDIZATION

There was a lot of talk about standardizing definitions, which helps set the stage for benchmarking, he said, adding that "it also helps set the stage to ensure there's parity on how FDA administers the program."

Greer stressed, however, that standardization adds cost to metrics reporting due to the work required to conform to a harmonized definition.

Three work-arounds were discussed:

- Firms could start with their own company definitions and transition to standardized definitions over time;
- Firms could simply measure their performance against their own metrics; or
- They could work to develop different sets of definitions that were more reasonable for each industry sector.

"Perhaps there are some common high-level things that apply across, but then specifically, within a sector, there may be more meaningful metrics or definitions or approaches that could be applied that really drive more value within that sector," he explained.

SHOULD INDUSTRY DIVE IN OR WAIT AND SEE?

Steve Mendivil, a senior advisor for Amgen, said it's a lot of work to align a company's internal measures to FDA's proposed quality metrics. For that reason, he asked whether companies wanting to participate in the fast-approaching voluntary phase of FDA's quality metrics program should just dive in and align to the revised draft guidance or wait to see if there is further clarification. "We hate to have to go through this internal revision twice."

"That's a tough one," said FDA's Jennifer Maguire. She had helped facilitate the conference's quality metrics workshop sessions, where, she said, "it seemed to be almost a 50% split on the folks who had the opinion that we should standardize the definitions and the folks who had the opinion that we should allow individual company-driven metrics. So, I think this is an area where we're going to need to have more dialogue. I wouldn't want to lead you astray."

Maguire added that the menu approach to quality metrics "greatly inhibits our ability to then use those metrics."

That and the uncertainty around how many companies will volunteer to participate "reduces our ability to really learn from the program and get some utility out of it," she said.

"It's a good question," Maguire concluded. "I think this is one of the top questions that we're going to have continuous dialogue on to figure out the best path forward."

From the editors of the Gold Sheet.
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FDA Announces Plans To Develop Supply Chain Security Pilot Program

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FDA plans to establish a pilot program, with the input of the pharmaceutical industry, to help it develop an electronic, interoperable system that will track and trace prescription drugs through the supply chain, the agency said in a July 20 Federal Register notice.

But first FDA wants to get an estimate from industry on the time involved in participating, according to the notice.

FDA also July 20 issued a notice of upcoming meetings on Drug Supply Chain Security Act (DSCSA) implementation.

DSCSA, signed into law on Nov. 27, 2013, outlines steps for building an electronic, interoperable system that will identify and trace certain prescription drugs as they are distributed within the US. This system must be in place by Nov. 27, 2023.

The law requires FDA to establish a pilot program, in coordination with manufacturers, repackagers, wholesale distributors and dispensers, to explore and evaluate methods to enhance the safety and security of the pharmaceutical distribution supply chain. The law also requires FDA to hold public meetings to explore issues affecting the supply chain and to provide opportunities for comment from stakeholders.

FDA has identified several potential issues to examine, and evaluation methods to use, in pilot projects established under the DSCSA pilot. These issues, which emerged from an FDA workshop held last year, relate to the product identifier and examining processes related to the requirement for manufacturers to affix or imprint a product identifier to each package.

Other issues pertain to barcode quality and examining the readability of the barcode, and the application of linear and 2D barcodes on products. Another area is exception handling and potential issues to examine include to identify honest errors such as over- or under-shipments.

The selected participants should be ready to start within four months of receiving a letter of acceptance from FDA, and the pilot will run for six months. In addition, the selected participants must be responsible for covering their own expenses associated with the pilot.

The announcement describes the proposed DSCSA pilot program including instructions for submitting a request to participate. FDA is soliciting comments on the proposed collection of information associated before submitting the proposed collection to the Office of Management and Budget for approval. FDA does not intend to begin the pilot or accept requests to participate until OMB has approved the collection of information.

FDA estimates that each respondent will spend eight hours coordinating with each partnering entity. For eight respondents with an average of two partnering entities, the estimated total burden for coordinating with partnering entities is 128 hours.

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> DSCSA outlines steps for building an electronic, interoperable system to identify and trace certain prescription drugs distributed within the US. It must be in place by Nov. 27, 2023.

The deadline for comment on the information request is Sept. 20. Comments can be submitted to https://www.regulations.gov and must reference docket No. FDA-2016-N-0407.

FDA also announced three upcoming public meetings to allow industry the opportunity to provide input on and develop strategies for the drug distribution security provisions of DSCSA. The announcement said that public meetings will be held on Aug. 23, 2017, Dec. 5 and Feb. 28. The meetings will be held at FDA's White Oak Campus in Silver Spring, Md.

The first public meeting will focus on supply chain security in 2023 and enhanced drug distribution security needs. The second public meeting will focus on electronic interoperability, standards for data exchange, data architecture, aggregation and inference. The third meeting will focus on a further refinement of enhanced drug distribution security needs and building capacity for a unit-level system.

Submit comments electronically, including attachments, to https://www.regulations.gov/, docket No. FDA-2017-N-3857. If your comments have any confidential information that you do not wish to be made available to the public, submit them on paper to Dockets Management Staff, (HFA)-305), FDA, 5630 Fisher's Lane, Room 1061, Rockville, Md. 20852.

From the editors of the Gold Sheet. Published online July 20, 2017

International Headwinds Counter J&J's Consumer Growth Confidence

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Johnson & Johnson is looking to products new to its consumer health portfolio and others new to its OTC brand lines to drive growth with an eye also on how foreign currency exchange and international regulations could slow the business.

"We're seeing some much weaker markets and some macroeconomic conditions, particularly in China and India, so we've adjusted our expectations," says Chief Financial Officer Dominic Caruso.

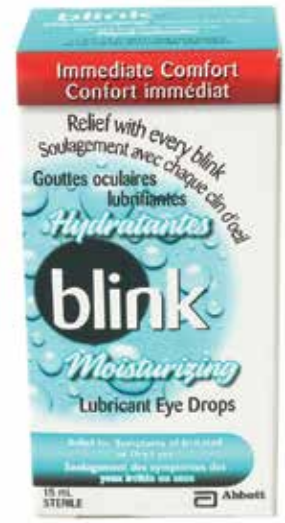
J&J on July 18 reported that sales of *Blink* eye drops and *Complete* contact lens solution, among the lines acquired from an **Abbott Laboratories Inc.** business earlier in 2017, and consumer response to advertising for *Tylenol* (acetaminophen) Rapid Release Gels contributed to 1.7% growth in consumer business revenues to $3.5bn in its fiscal 2017 second quarter.

However, currency exchange rates sliced 1.1% from consumer revenue growth, though the firm and analysts see relief on the currency horizon. J&J describes the 2017 outlook as "a smaller negative impact" from currency exchange, while Leerink analysts in a same-day research note advised that the firm "confirmed that currency is becoming less of a headwind for the company for its international sales."

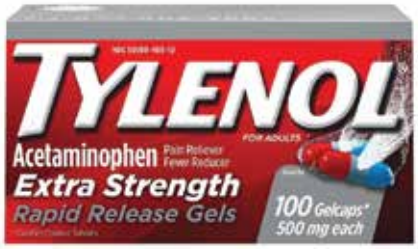
Chances for improvements in its China and India outlook aren't as strong, though. China's fluid regulatory framework is constraining distribution by international pharma firms and India's limit on available currency denominations is hitting many consumer product categories.

"We've got to get through some of these policy issues in India related to demonetization. There's something in the way that OTC and pharma drugs are being distributed that we've got to get through in China," said J&J CEO Alex Gorsky during the firm's earnings briefing analysts.

J&J won't get through those unscathed, analysts caution. In July 19 notes, BMO Capital Markets analyst Joanne Wuensch says "the macro environment and policy constraints in China and India are likely to weigh on" J&J's consumer business, and Deutsch Bank's Brittany Henderson says "conditions in India and China was the bulk of the company's" reason for lowering its constant currency forecast for 2017.



The Blink eye drops line and other former Abbott Medical Optics' consumer brands accounted for $25m in J&J's second-quarter consumer health revenues.



Sales of Tylenol Rapid Release Gels got a boost from TV and online advertising highlighting the product's "laser-drilled holes" designed to accelerate the release of acetaminophen.

Sales in India also were negatively impacted by the country's implementation of a national goods and services tax, which "resulted in some market disruption," said J&J Investor Relations Vice President Joseph Wolk.

About the forecast change, Wolk said "we did tighten up our range on operational or constant currency sales a little bit, lowered that midpoint just a bit" to a rate of 7% to 8%.

LINE EXTENSIONS DON'T MOVE BOTTOM LINE

J&J executives and analysts alike note the firm's pending OTC brand line extensions as key drivers for 2017 second-half sales growth, but the firm isn't saying which lines are expanding while it is saying the additional revenues won't boost its bottom line.

A J&J spokesman said the consumer business has not disclosed the brands it will be expanding during the remainder of 2017.

Still, CFO Caruso said J&J is boosting consumer business spending to support its brand expansions, and "we still expect new product launches in consumer to have a meaningful positive impact on second half growth."

Like all other consumer business earnings and forecast reports J&J provided, the pending product launches were discussed with a note of caution, including that the company typically returns some of the revenue gains from portfolio extensions to the business.

Product launches will be in "weaker markets" and their "positive impact will be mitigated to some extent, Caruso said. "The impact from the weaker macroeconomic dynamics in consumer is now estimated to continue through the balance of the year longer than we have previously expected."

Gorsky acknowledges J&J's challenges on the consumer and other pharma and medical device fronts, but also says what's not to like about the firm's "world-class portfolio of iconic mega brands" in the OTC

and other consumer health sectors.

J&J's history of backing products with science "helps translates into very strong brand images" across its consumer portfolio, he said, adding, " while we have seen some recent slowdowns in some of the markets … we think at the end of the day, we're still going to need products to fill all these channels."

CHANNEL VISION WIDENS

J&J is filling more consumer vision care channels since closing its $4.3m acquisition of **Abbott Medical Optics Inc.** in February. *(Also see "J&J Buys Abbott's Ophthalmics Business For $4bn-Plus" - Medtech Insight, 16 Sep, 2016.)*

Former Abbott Medical consumer lines Blink eye drops and Complete multi-purpose contact solution account for $25m in J&J"s consumer health revenues in "the first full quarter we are reporting for that," Wolk said.

Overall OTC drug sales during the April-June period grew 2.1% to $1bn excluding foreign exchange impact. Zyrtec (cetirizine/pseudoephedrine) allergy line sales grew 17% worldwide, though about two-thirds of the growth was from US distributors restocking inventory during a comparatively late allergy season.

Sales of Tylenol Rapid Release Gels 500mg got a boost from TV and online advertising highlighting the product's "laser-drilled holes" designed to accelerate the release of acetaminophen once taken. The product design isn't new but the ad promoting the design is, J&J's spokesman said.

J&J said its worldwide oral care product sales were impacted by 1% market contraction from the year-ago quarter and slipped slightly to $396m.

Its personal care, or beauty lines grew 10.2%, with 17.1% US growth offset by a lower increase of 1.2% internationally, to $1.08bn. J&J noted $94m sales of *Vogue* products, estimated pro forma "to have grown high single digits" since the firm acquired the line in 2016. *(Also see "J&J Invests In Consumer Business For Long Haul, Not Quick Sale" - Pink Sheet, 16 Sep, 2016.)*

From the editors of the Tan Sheet.
Published online July 19, 2017

India Mulls Contentious Move To All 'Vegetarian' Pharma Capsules

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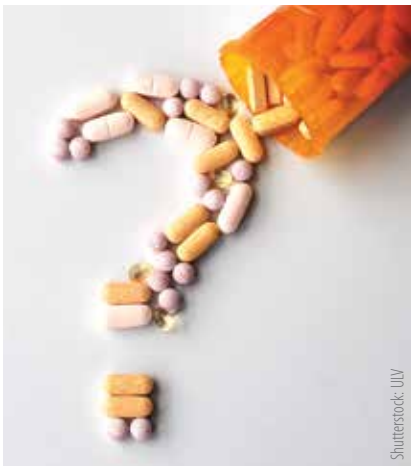
Two years ago, a government scientific advisory committee in India approved in principle a switch to cellulose-based capsules from gelatin. Now an expert committee set up by the country's health ministry is seeking to "address all technical issues pertaining to replacement of gelatin capsules", and Health Minister J.P. Nadda has said "necessary steps" toward adopting plant-based capsules should "be taken on priority."

But opposition from industry, a lack of Indian cellulose suppliers, the plant-based capsules' much higher cost, and domestic and foreign regulatory requirements may still weigh heavily against any immediate implementation of the plan, observers say.

The proposal to shift to cellulose capsules is being championed by prominent animal rights' activist Maneka Gandhi, who serves as women's development minister in the Hindu nationalist government of Prime Minister Narendra Modi. "In a country where there are millions of vegetarians, this [gelatin capsules] hurts religious sentiments and many people avoid medicines that are in capsule form," Gandhi wrote in a letter to Nadda, pressing for action.

The Drug Controller General of India, G.N. Singh, who's tasked with overseeing the country's drug regulatory industry, has also declared he favors the idea, saying: "Vegetable capsule for vegetarian society." Some 29% of India's 1.25 billion people, mainly those belonging to the majority Hindu religion, are vegetarian, according to a 2014 census study. But other Hindus, along with minority Muslims and Christians, eat meat.

Indian industry groups have reacted with dismay to the proposal to switch to plant-origin capsules. The Punjab Haryana Delhi Chamber of Commerce in North India, whose membership manufactures 95% of the gelatin made domestically, and drug makers say adoption of the plan could be disastrous. India's capsule industry is valued at around INR50bn ($780m).



"The proposal is completely impractical and ill-advised." – Vivek Seigell, PHD Chamber of Commerce director

"The proposal is completely impractical and ill-advised," PHD Chamber of Commerce director Vivek Seigell told the *Pink Sheet* on July 17. "We have no idea of the cost of such a change. Also, getting all medicines certified as safe and effective in plant-based capsules both nationally and internationally – it would be a Herculean task that would take years," he said.

EXTENSIVE TESTS NEEDED TO ESTABLISH EQUIVALENCY

Cellulose capsules are mainly used for herbal and nutritional products, not for antibiotics, oncology, anti-infectives, painkillers or other medicinal drugs,

Seigell noted. Tests would need to be conducted on whether such medicines could maintain their stability, bioavailability, bioequivalence and other properties if packaged in cellulose capsules, he said.

At present, 95% of capsules used worldwide are gelatin and the figure is even higher in India at 98%, the PHD chamber said. Gelatin is made by boiling the tissues, bones and skin of animals, normally cattle and pigs. In India, though, cows are considered sacred by many Hindus, while Islam forbids pork consumption. Due to these issues, Indian gelatin makers say they use bones of buffaloes, which are not considered holy by Hindus.

India is constitutionally secular but since the 2014 election of Modi's government, Hindu hardliners have been pushing assertively for laws to be framed in accordance with Hindu religious beliefs. Amid a swell of Hindu nationalism, Modi's government in May banned trade of cattle for slaughter, dealing a major blow to the country's thriving meat exports trade. The government included buffaloes in its prohibition, saying many cows were being clandestinely slaughtered alongside buffaloes.

The Supreme Court has suspended the order but the cattle trade's future remains uncertain and shortages of gelatin supplies have been reported. Cow protection is an emotive, highly charged issue and simmering tensions have sometimes flared into mob lynchings of people suspected of storing beef or transporting cattle for slaughter.

The health ministry originally suggested plant-based capsules carry green dots and meat-derived ones red dots. But the government's Drug Technical Advisory Board dismissed the idea, noting "drugs are not taken for choice but are prescribed by doctors to save lives and marking them as vegetarian or non-vegetarian origin is not desirable."

The PHD Chamber of Commerce agreed, saying, "It is not prudent to enter the vegetarian and non-vegetarian debate in this matter. The group also argued that gelatin used for capsules was processed from leftover bones and no animals were killed expressly.

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ALTERNATIVES, COSTS, DATA

The ministry is looking specifically at making capsules from hydroxpropyl methylcellulose (HPMC). Capsules can also be made from other plant materials such as starch but HPMC capsules offer various technical benefits including low-moisture content. According to the September 2016 issue of Tablets & Capsules Magazine, pharmaceutical and nutraceutical developers are increasingly using HPMC capsules for new products. HPMC capsules are forecast to hold 9-10% of the capsule market by 2019, up from 3-4% in 2014.

Still, in a recent three-year period, just three of 29 capsule drug products approved by FDA used an HPMC capsule, the trade publication said.

"The investments required to be made for manufacturing cellulose-based capsules are substantial and will require planning and time," the PHD Chamber of Commerce said. The cost of raw material required to make cellulose capsules is "approximately four times that of gelatin and the manufacturing cost of cellulose-based capsules approximately three times the cost of gelatin capsules," the chamber said.

The Indian Drug Manufacturers' Association, meanwhile, argued that gelatin capsules, in use for over a century, are the "mainstay of drug delivery systems for safety, convenience…and pharmacokinetic parameters" and have been approved by US, European, Indian and other regulators.

Plant-based capsules "do not have time-tested data," the association said. The idea "should not be considered casually… without considering in-depth the scientific, technical, techno-commercial, availability and affordability issues. This could impact all the citizens of this country, as also globally as most countries are dependent on India's quality, affordable generic drugs," the group advised.

EXPORTS IMPACT?

India, a low-cost production hub, is the largest provider of generic medicines globally, supplying 30% of US generic imports. Mandating plant-based capsules could "totally disrupt our export market," the association warned. The capsule debate comes as India's drug industry faces an uncertain future, beset by slowing revenues especially in its largest US market, fierce competition and regulatory worries.

Critics of the move say that if the government really wants to go ahead with plant-origins capsules, it should prepare a multi-year roadmap rather than take any abrupt steps.

Drug controller Singh has acknowledged that "the stability, bioequivalence of the drugs have to be established for the Indian as well as export market" to meet regulatory requirements. Also, costlier capsules would go against the Modi government's stated aim of making drugs more affordable in a country where tens of millions of Indians are pushed into poverty each year by medical expenses.

"The government will do well to guard against pandering to 'religious sentiments' on health matters," the Indian Express newspaper remarked in a recent editorial.

From the editors of PharmAsia News.
Published online July 19, 2017

China Expects Earlier Start Of National Marketing Authorization Holder System

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Since the Drug Marketing Authorization Holder (MAH) system was rolled out in 10 provinces in China under a trial program last year, coupled with support from local financial subsidies, China's FDA had received 381 MAH applications by June this year, including some for global novel drugs.

Given the positive feedback, the new system is now expected to be promoted nationwide, and the details of implementation are under development, CFDA's officers disclosed at a recent MAH summit in Shanghai.

China's State Council officially issued the trial plan for MAH system on 26 May 2016 for the 10 provinces - Beijing, Tianjin, Hebei, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Sichuan - encouraging pharmaceutical research institutions and individual researchers from these areas to submit applications for clinical trials or marketing authorization registration. *(Also see "Authorization Holder Scheme To Shake Up China R&D, Production" - Scrip, 5 Nov, 2015.)*

PILOT PLAN PROMOTING INNOVATIONS

As of May 31, CFDA had accepted a total of 381 applications, most of which came from Jiangsu, Zhejiang, Guangdong, Shandong and Sichuan, accounting for 93% of the number, but only one filing from an individual researcher, said Sheng Yang, the deputy director of the Department of Drug and Cosmetics Registration at CFDA, at the summit.

Shanghai stands out among the rest, with 24 applications from 16 Shanghai-based companies and organizations, notably including nine global innovative drugs in Class 1.1 with independent intellectual property rights for oncology and diabetes indications, noted Raoshui Chen, deputy director of the Shanghai FDA, giving an example of **Hutchison China MediTech Ltd.**'s anticancer drug fruquintinib (HMPL-013).

Currently, most of the applications were filed for clinical trial approvals, numbering 171 filings, while there were 126 applications filed for marketing authorizations. Most of the applicants were still pharmaceutical manufacturers, which accounted for 63% of the total, and research institutions came next, making up 37% of the applicants.

"Research institutions have increased significantly in the application filings, in other words, these 142 research institutions without production capacity would have had to sell their research accomplishments in the past," Yang said. "But now under the support the MAH system, they can outsource the manufacturing process to professional organizations and have a drive to focus on continuing the development."

The trend of increasing applications from research institutions was more obvious in Shanghai, as 12 out of 16 applicants were institutions, resulting from its various biopharmaceutical clusters, Chen noted.

SIGNIFICANT COST SAVINGS

After the one-year pilot program, the policy also seems to be attracting and inspiring returnees to bring home with innovative products, the CFDA's Yang said. "The MAH pilot plan has allocated resources more efficiently to avoid duplicated constructions, and has reduced about CNY1bn [$142m] in fixed assets investment."

Li Chen, CEO of Shanghai-based **Hua Medicine Ltd.**, echoed that the MAH designation it has been granted has greatly helped to develop its novel glucokinase activator HMS5552 for type 2 diabetes.

"Our big concern was how to manufacture the drug for Phase III trials," Chen explained. "It was impossible for us to spend CNY200m to build a manufacturing plant before finishing Phase II, but it would be too late to start the construction after Phase II, which could take two to three years, when we are running against **Pfizer Inc.** and **Eli Lilly & Co.** in developing novel drugs under the same indication."

Shanghai Syn-The-All Pharmaceutical, a contract manufacturing organization (CMO) subsidiary under **WuXi AppTec Inc.**, has also seen the MAH policy promote its business, as pharma firms pursue strategic transformation without establishing additional production lines.

Mingzhang Chen, CEO of Syn-The-All Pharmaceutical, noted that the company has been manufacturing more than 40 products at Phase III and commercialization stages, including some global blockbuster drugs, such as **AbbVie Inc.**'s *Imbruvica* (Ibrutinib) and **Tesaro Inc.**'s *Zejula* (niraparib). The company is also responsible for producing three drugs from the first batch of 12 MAH pilot drugs, Chen added.

HOW FAR FROM EXPANDING NATIONWIDE?

Since the results of the pilot plan have been revealed, the industry eagerly looks forward to promoting the MAH system in the whole country, and the CFDA officer also sent out a promising signal.

"CFDA is considering to fully implement the MAH system at the provincial level in developed areas as a first step, and will give a full report to the National People 's Congress. Once approved we will shift the law amendment procedure to an earlier date," Yang said.

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"CFDA is open to companies for discussion on the MAH details in terms of interprovincial implementation, segmented production outsourcing and biologic manufacturing," he added.

To ensure the national implementation of the MAH system requires continuous testing in the pilot areas, and Shanghai, as the first province with detailed rules, has carried out a "risk relief system" to back MAH holder companies.

The Shanghai Zhangjiang Hi-Tech Park committee set up a CNY50m insurance fund managed by a third party. At the same time, the committee also invited Chubb Limited, China Pacific Insurance Company and PingAn Insurance to provide commercial liability schemes, offering several insurance plans for the MAH holders.

Shanghai FDA's Chen disclosed that companies also can get supportive allowance to buy liability insurance, listing Hua Medicine, **Zai Lab Ltd.**, **Hutchison MediPharma Ltd.**, and Haihe Biopharm.

To better support the MAH system, Shanghai established another national biopharmaceutical cluster in Jinshan district of 1.2 million square meters, where it has already developed three innovative drugs under the pilot plan and is able to provide services for the whole industry chain from API, biological agents, pharmaceutical intermediates and excipients to diagnostic research.

From the editors of PharmAsia News. Published online July 20, 2017

FDA's NDA And BLA Approvals: Zypitamag, Nerlynx, Vosevi, Lusduna

Below are FDA's original approvals of NDAs and BLAs issued in the past week. Please see key below chart for a guide to frequently used abbreviations

SPONSOR	PRODUCT	INDICATION	CODE	APPROVAL DATE
New Drugs				
Zydus	*Zypitamag* (pitavastin)	Treatment of patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, triglycerides, and to increase high-density lipoprotein cholesterol.	S, 2	7/14/2017
Puma	*Nerlynx* (neratinib)	Extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab based therapy.	S, 1	7/17/2017
Gilead	*Vosevi* (sofosbuvir/ velpatasvir/ voxilaprevir)	Fixed-dose combination for the treatment of adult patients with chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) who have 1) genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor or 2) genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor.	P, 1, 4	7/18/2017
Merck	*Lusduna* (insulin glargine)	Tentative approval, pending resolution of patient infringement regulation, of the Lantus copy for diabetes treatment. *(Also see "Merck's Lantus Copy Lusduna Poised For US Market Pending Litigation" - Scrip, 20 Jul, 2017.)*	S, 5	7/18/2017

KEY TO ABBREVIATIONS	
Review Classifications	**NDA Submission Classification**
P: Priority review **S:** Standard review **O:** Orphan Drug	**1:** New molecular entity (NME); **2:** New active ingredient; **3:** New dosage form; **4:** New Combination; **5:** New formulation or new manufacturer; **6:** New indication; **7:** Drug already marketed without an approved NDA; **8:** OTC (over-the-counter) switch; **9:** New indication submitted as distinct NDA – consolidated with original NDA; **10:** New indication submitted as distinct NDA – not consolidated with original NDA

Recent And Upcoming FDA Advisory Committee Meetings

TOPIC	ADVISORY COMMITTEE	DATE
Intellipharmaceutics Corp.'s oxycodone extended-release tablets, with purported abuse-deterrent properties, for management of moderate-to-severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time	Anesthetic and Analgesic Drug Products/Drug Safety and Risk Management	July 26
Safety and efficacy of Dynavax's hepatitis B vaccine	Vaccines and Related Biological Products	July 28
Janssen Biotech's *Plivensia* (sirukumab) for adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or are intolerant to one or more disease-modifying anti-rheumatic drugs	Arthritis	August 2
Pfizer's *Xeljanz* (tofacitinib) for treatment of adults with active psoriatic arthritis	Arthritis	August 3

Pink Sheet

LEADERSHIP
Phil Jarvis, Mike Ward

CORPORATE SALES
John Lucas, Elissa Langer

ADVERTISING
Christopher Keeling

DESIGN
Jean Marie Smith

US
Denise Peterson
Nielsen Hobbs
Mary Jo Laffler

Europe
Eleanor Malone
Maureen Kenny
Alex Shimmings

Asia
Ian Haydock

POLICY AND REGULATORY

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Michael Cipriano
Bowman Cox
Joanne Eglovitch
Eileen Francis
Derrick Gingery
Cathy Kelly
Brenda Sandburg

Bridget Silverman
Malcolm Spicer
Sue Sutter

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Neena Brizmohun
Ian Schofield
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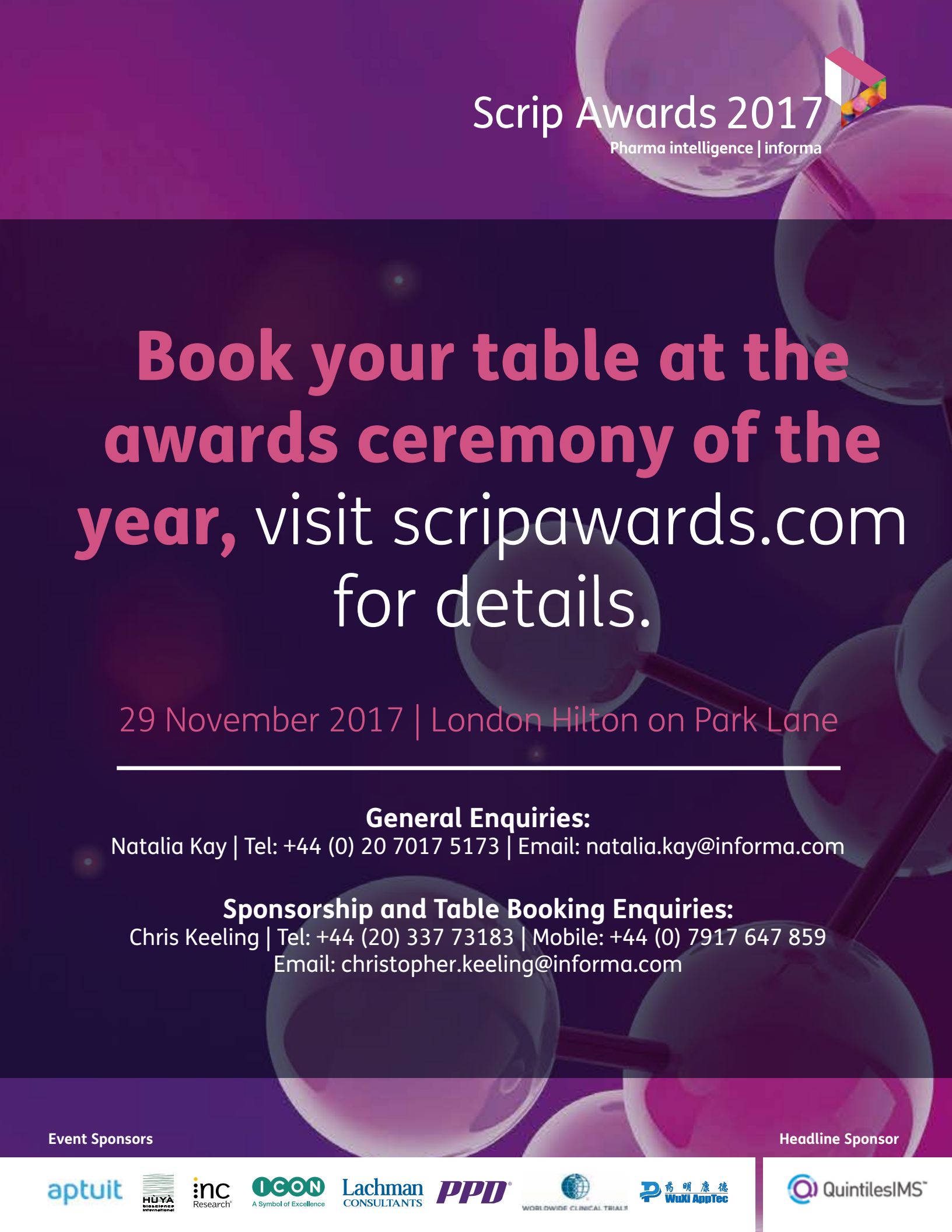
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