Welcome to the July 2021 DIA Regulatory Affairs Community AdPromo Working Group

Web Meeting

July 14, 2021

Your WG Chairs: Kimberly Belsky (Mallinckrodt Pharmaceuticals) and Renee Ambrosio (Merck & Co., Inc.)

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Reminder - Please Mute Your Line if You are Not Speaking Thank you!

Hold the Dates! The DIA AdPromo WG will generally meet on the 3rd Wednesday of each month at 12:00 pm eastern

August 11 @ 12 pm - 1 pm ET (NOTE: This is the 2nd Wednesday of the Month)	**HOLD the Date! Topics to follow**	**Join the Zoom Meeting** https://diaglobal.zoom.us/j/96130432143 **Meeting ID: 961 3043 2143**
September 8 @ 12 pm - 1 pm ET (NOTE: This is the 2nd Wednesday of the Month)	**EU Medical Device Regulation – "Everything Connected Everything - How the MDR and IVDR Up the Game for Claims for Devices"– *Erik Vollebregt, Axon Lawyers***	**Join the Zoom Meeting** https://diaglobal.zoom.us/j/95730615492 Meeting ID: 957 3061 5492
October 20 @ 12 pm - 1 pm ET	**Enforcement Letters – Q&A on The Process and Insights -*Bob Dean (Merck) & Mark Gaydos (Sanofi)***	**Zoom info to follow**

Today's Agenda

- **Drug Pricing Disclosure in Ads --- *A Comeback?***
- **OPDP Research: Medical Conference Attendees' Observations About Rx Drug Promotion**
- **CDRH Warning Letter issued for AQUAGOLD® *fine touch* and the Advanced Skin Application Platform (A.S.A.P!) Micro Infusion System**
- ***Guest Presenter!* The Role of Regulatory Information Management in Promotional Material Compliance *-Kathie Clark, Ennov***

Senators Revive Bill to Include List Prices After GAO Report Published

DTC ads may contribute to an increase in Medicare drug spending, but it is difficult to tease out how much of an impact it has, a new General Accountability Office report shows.

- **A new May 2021 U.S. Government Accountability Office report on** Medicare Spending on Drugs with DTC Advertising **found drugmakers spent $8.2 billion of the $17.8 billion from 2016-2018 on DTC ads for drugs in three therapeutic categories: inflammatory conditions, endocrine and metabolic disorders, and conditions affecting the central nervous system**
  - The report examines (1) drug manufacturer spending on DTCA; (2) Medicare spending on advertised drugs; and (3) changes in DTCA spending and Medicare use and spending for selected drug
- **The report pushed U.S. Senate Majority Whip Dick Durbin, D-Ill., and Sen. Chuck Grassley, R-Iowa, to reintroduce legislation that would require drugmakers to disclose prices in ads**
  - They requested the GAO report and said its findings confirm the need for reforms

Endpoints News (free reg. req'd) (6/18/21) • U.S. Government Accountability Office (6/17/21) • Read the report (5/18/21

Senators Revive Bill to Include List Prices After GAO Report Published

Examples from the Report… take note of the dates and other factors

- *GAO found ad spending on Eliquis increased by over $150m from 2013 to 2016. At the same time, the number of Medicare Part D beneficiaries using the drug grew from almost 47,000 to about 827,000 and Part D spending rose from $45m to $1.9bn, according to the report.*

- *Similarly, from 2013 through 2015, AbbVie increased DTC ad spending for Namenda XR by almost $76m, the number of Part D beneficiaries using the drug grew by almost 300,000 and Part D spending increased over 20-fold, from $46m to $952m*

- **GAO cautioned that "while these examples illustrate how consumer advertising may contribute to increased Medicare use, events such as [US Food and Drug Administration] approval for additional indications would have likely led to increases in drug use on their own."**
  - Stakeholders interviewed by **GAO "cited a number of other factors that likely contribute to the overall use of drugs and drug spending**, including in Medicare," the report notes. **They include doctors' prescribing decisions, health plan formulary controls, a drug's therapeutic benefit and manufacturer spending on drug promotions directed to doctors**.

OPDP Research Medical Conference Attendees' Observations About Prescription Drug Promotion

- **Announced in the Federal Register July 14, 2021**
  - FR Notice with comments/responses following initial announcement in FR in September 2020
  - Comment close August 13, 2021

- **Research Overview and Goals**
  - (1) Focuses on understanding the landscape of HCP-directed promotion of Rx drugs at medical conferences in general and, more specifically, **how elements of pharmaceutical booths in medical conference exhibit halls impact HCP attendees' perceptions of the drugs that are promoted at those booths**
    - FDA will first ask attendees who are prescribers within different disciplines (primary care physicians, specialists, nurse practitioners, and physician assistants) general questions about their attendance at medical conferences, including questions about their motivations for attending, activities they participate in (*e.g.,* symposia, poster sessions, social events, exhibit halls), and their opinions about the Rx drug treatments promoted at medical conferences.
  - (2) **The second part will allow OPDP to get more detailed information about interactions in medical conference exhibit halls**
    - A 2006 study found that at least 80% of physicians attended at least 1 medical conference each year and spent an average of 7 hours on the exhibit hall floor at each event
    - **The length of time spent at each booth—between 12 and 21 minutes—was comparatively longer than detailing visits in HCP offices, which range from 5 to 10 minutes on average. Thus, medical conference exhibit booths provide opportunities for pharmaceutical companies to market to large numbers of HCPs and potentially engage in more lengthy interactions.**

OPDP Research Medical Conference Attendees' Observations About Prescription Drug Promotion

- **This study is designed to provide insights to inform the advisory comments that OPDP provides to pharmaceutical companies that voluntarily seek FDA review**.
  - **Recent compliance letters issued by OPDP described booth or panel displays that communicated misleading information** regarding drug efficacy and safety, provided insufficient information on drug risks, and omitted "material facts" about the promoted drug
  - A primary reason that physicians and other medical professionals report visiting specific exhibitors at conferences is to obtain product information, and it is important that the information provided by exhibitors to HCPs regarding the risks and efficacy of prescription medications not be false or misleading. Thus, investigating the impact of pharmaceutical booth promotions among medical conference attendees has valuable practical implications for the public health

OPDP Research Medical Conference Attendees' Observations About Prescription Drug Promotion

- **Excerpt of Comments Submitted and OPDP Responses (n=25)**
  - **(Comment 11) One comment suggested the inclusion of additional questions about the perceived credibility of the booth representative**, the likelihood of recommending the prescription drug, or the desire to conduct further inquiries for the product.
    - (Response 11) We have included questions about booth representative credibility and intention to prescribe
  - **(Comment 25) One comment recommended the addition of a choice that reads, "met with the sales representative virtually,"** for Question 51, as this has been occurring more frequently during the COVID-19 pandemic.
    - (Response 25) This response option was added

CDRH Warning Letter Issued to Aquavit Pharmaceuticals for Promotional Claims

- **FDA CDRH Warning Letter issued to Aquavit Pharmaceuticals for the marketing the AQUAGOLD® *fine touch* and the Advanced Skin Application Platform (A.S.A.P!) Micro Infusion System without marketing clearance or approval**
  - Date of Warning Letter 6/17/2021 based on claims made on the product websites *(posted 6/29/2021)*

- Per the websites, https://aquagoldfinetouch.com and https://skinworkout.com the AQUAGOLD® *fine touch* is a **microchannel microinjector available for physician and clinical practitioner use that delivers "specially selected therapeutics" into the dermis to address a wide range of skin concerns**, and the A.S.A.P! Micro Infusion System is a **microchannel applicator designed for at-home use to deliver microdroplets of treatment solutions** directly into the skin

- Based on claims, the AQUAGOLD® fine touch is a device because it is **intended to deliver microdoses and microinjections of products into the skin for various medical purposes** (e.g., stimulating collagen and elastin production, promoting wound healing, treating acne scars, hyperhidrosis, and alopecia)

• ***"How is AQUAGOLD® fine touch™ different from microneedle devices?*** *The intended use of AQUAGOLD® fine touch™ is to microdose and microinject, whereas the intended use of other common microneedle devices is to puncture or wound the skin."*

• ***"MORE THAN JUST NEEDLING[:]*** *The microchannel screw-like design safely and consistently delivers therapeutics at a consistent depth with minimal damage to the dermis, targeting all layers of the skin while stimulating collagen and elastin production."*

• ***"UNIQUE 2-IN-1 TREATMENt[:]*** *Targeted treatments that include a wound-healing response, and simultaneously stimulate collagen and elastin production."*

• ***"PERSONALIZED MEDICINE[:]*** *Specially selected therapeutics for a treatment customized just for you. Address a wide range of skin concerns from acne scars and fine lines to hyperhydrosis and alopecia."*

CDRH Warning Letter Issued to Aquavit Pharmaceuticals for Promotional Claims

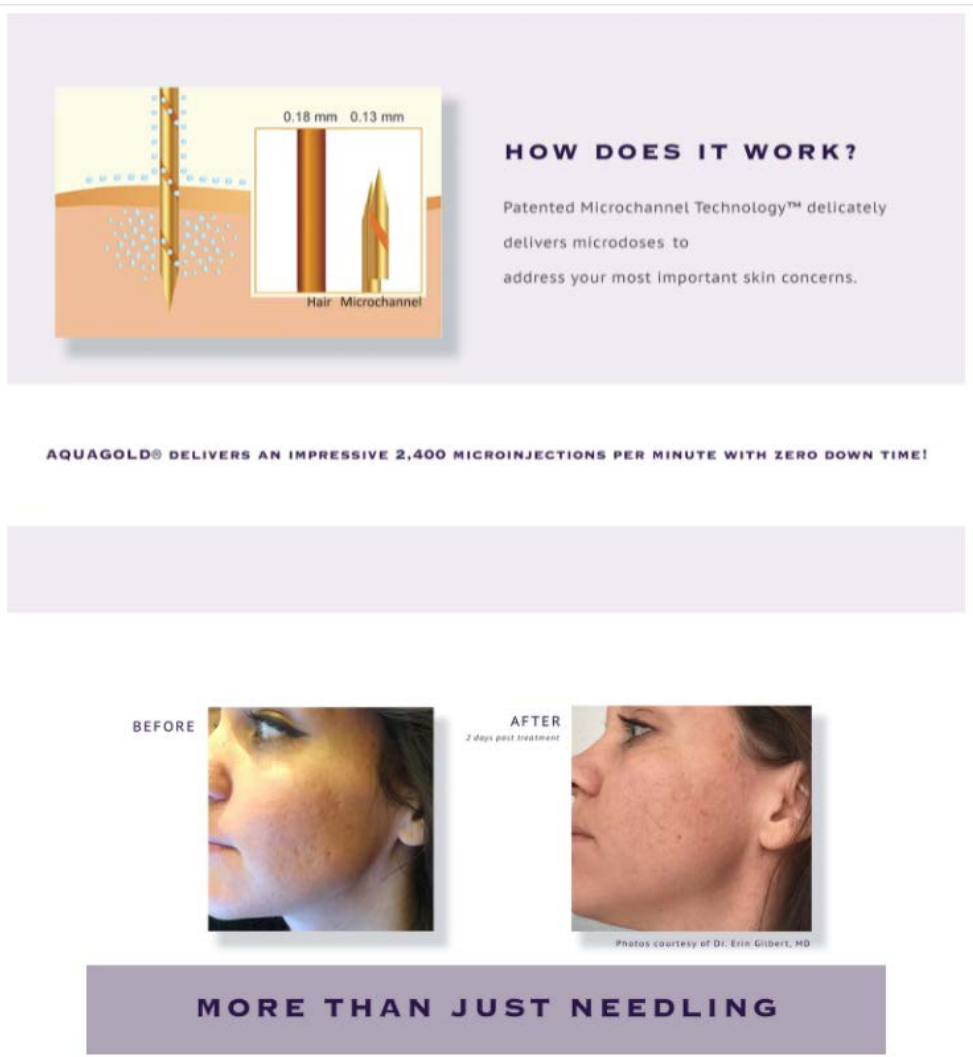
- ***The Issue(s)*** *(excerpt)*
  - Microneedling devices for aesthetic use are **Class II devices regulated** under 21 CFR 878.4430 and **require premarket notification [510(k)]**.
    - At this time, no microneedling device has been cleared for OTC or home use.
    - Additionally, **devices intended for transdermal delivery of topical products such as cosmetics, drugs, or biological products are not included in this classification and may need to be evaluated by CBER and/or CDER (re: combo products)**
  - CDRH noted that **the firm is also marketing other products that are drugs, biological products and/or combination products**, which are subject to additional/different requirements than those discussed above.
    - For example, you are marketing the SKINWORKOUT® U.R. (Ultimate Radiance) and the SKINWORKOUT® T.T. (Targeted Toning) as serums that are intended to be injected into the human body for various medical purposes

- ***Prior communications with the company*****.** FDA had previous interactions with the firm regarding these products, including in correspondence related to: (1) **It Has Come To Our Attention (IHCTOA) letters** sent May 10, 2016 and July 18, 2016, (2) a Request For Designation (RFD) submitted to FDA on April 10, 2017, and (3) FDA's inspection from October 23, 2019 to December 19, 2019

- ***AND, there's guidance on this topic.*** FDA noted in the WL (footnotes), **Regulatory Considerations for Microneedling Products - Guidance for Industry and FDA Staff** (November 2020) to assist industry in understanding when a microneedling product is a device as defined in section 201(h) of the Act
  - The guidance discusses a **firm's claims and statements associated with a microneedling product that FDA believes would generally cause the product to meet the device definition (e.g., it treats scars, treats wrinkles and deep facial lines, treats acne, treats alopecia, stimulates collagen production, and promotes wound healing)**

CDRH Warning Letter Issued to Aquavit Pharmaceuticals for Promotional Claims

- ***A view.*** Website accessed June 29, 2021



https://aquagoldfinetouch.com/pages/aquagold

Guest Presenter!

The Role of Regulatory Information Management in Promotional Material Compliance

-Kathie Clark, Ennov

Kathie Clark is a Product Director for Ennov Software for Life. While at IQVIA, she led the design and development of IQVIA's ePromo solution, which manages the creation, review, expiry, withdrawal and tracking of promotional materials. She also has over 20 years of experience in Regulatory Information Management, Regulatory Content Management and Submission Publishing, including work to define rejection criteria and improve usability of review tools for FDA reviewers while at GlobalSubmit. Recently, she authored the Advertising and Promotional Materials chapter of the DIA RIM White Paper.

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Kathie Clark: About Me

- Product Manager for several regulated content solutions at Ennov Software for Life; contributor to RIM solutions
- Previously led the design and development of IQVIA ePromo solution for the management of the review, dissemination and withdrawal of promotional and medical materials
- Product manager, subject matter expert and solution consultant for regulatory consent management and publishing products at IQVIA, NextDocs, GlobalSubmit and First Consulting Group
- Worked with FDA reviewers to develop eCTD validation and reviewing tools while at GlobalSubmit
- Member of the RIM Reference Model White Paper Working Group
- https://www.linkedin.com/in/kathieclark/

Regulatory Information Management

“Regulatory Information Management refers to the effective and efficient identification, collection, curation, communication, and management of regulatory information for products across the life sciences value chain.”

-- **Regulatory Information Management Whitepaper V2.0,**

RIM and Promotional Materials: What are the Links?

Regulatory Intelligence. Understanding regulations; advising on what Health Authorities are likely to accept – or challenge?

Resources: Planning, providing and tracking resources for submissions, MLR review, etc.

Submissions. Planning, creating and submitting required Ad/Promo submissions for promotional materials.

Status. Understanding the submission and (if necessary) approval status of promotional and medical materials.

Regulatory Role in Ad/Promo

- Advise on strategy, suitability for audience, prescribing info, risk/balance, …
- Consult / liaise with Health Authorities
- Track market-specific regulations and respond to changes and new regs
- Participate in MLR Review
- Prepare and submit AdPromo submissions
- Track and report on submission status of specific pieces
- Monitor Health Authority enforcement actions such as “Bad Ad”; also competitors
- Create reports and metrics; analyze trends; plan resources

Submission and Approval Pathways

No Submission Required
Based on Health Authority and specific details, piece does not have to be submitted

Submission – No Approval
Piece must be submitted to a Health Authority, but no approval is needed

Submission - Approval
Piece must be submitted and cannot be used until approval explicitly granted

Tacit Approval
Piece must be submitted, but can be used after a specified time has elapsed unless notified by Health Authority

Submission Considerations: Defining the Process

- Roles and Responsibilities
- Process for providing documents/media and associated information and due dates
- Standing and/or ad-hoc schedules for submissions
- Tracking and reporting process
  - What was submitted and when
  - Status of materials; notification when they can be used/disseminated
  - When do materials expire and can they be extended
  - Whether materials are withdrawn
- Service Level Agreements

Submission Considerations: FDA

- Format: eCTD / electronic for almost all applicable submissions to FDA; other formats vary by market
- For FDA (eCTD) submissions, eSubmission tasks include:
  - Allocation of sequence numbers
  - Preparation and transmittal to publishing of Ad/Promo materials
  - Preparation of compliant forms and cover letters
  - Submission publishing
  - Submission via the Gateway

See Providing Regulatory Submissions in Electronic and Non-Electronic Format — Promotional Labeling and Advertising Materials for Human Prescription Drugs

RIM Technology

RIM systems can assist with a number of tasks related to Ad/Promo:

- Providing information about product status in each market
  - Approval status, planned and approved extensions/variations, approved indications and label
- Managing and tracking planned and completed submissions
- Tracking Health Authority correspondence
- Tracking status, submission (and approval) dates and expiration dates for promotional materials
- Integrating with Regulatory Intelligence
- Providing dashboards and metrics

RIM Metrics for AdPromo

MLR Review
MLR approval times, rework cycles and reasons

Delays
Percentage of activities (such as publication or sales launch) delayed due to late availability of promotional materials

Workload
Time spent in MLR review and in submission preparation

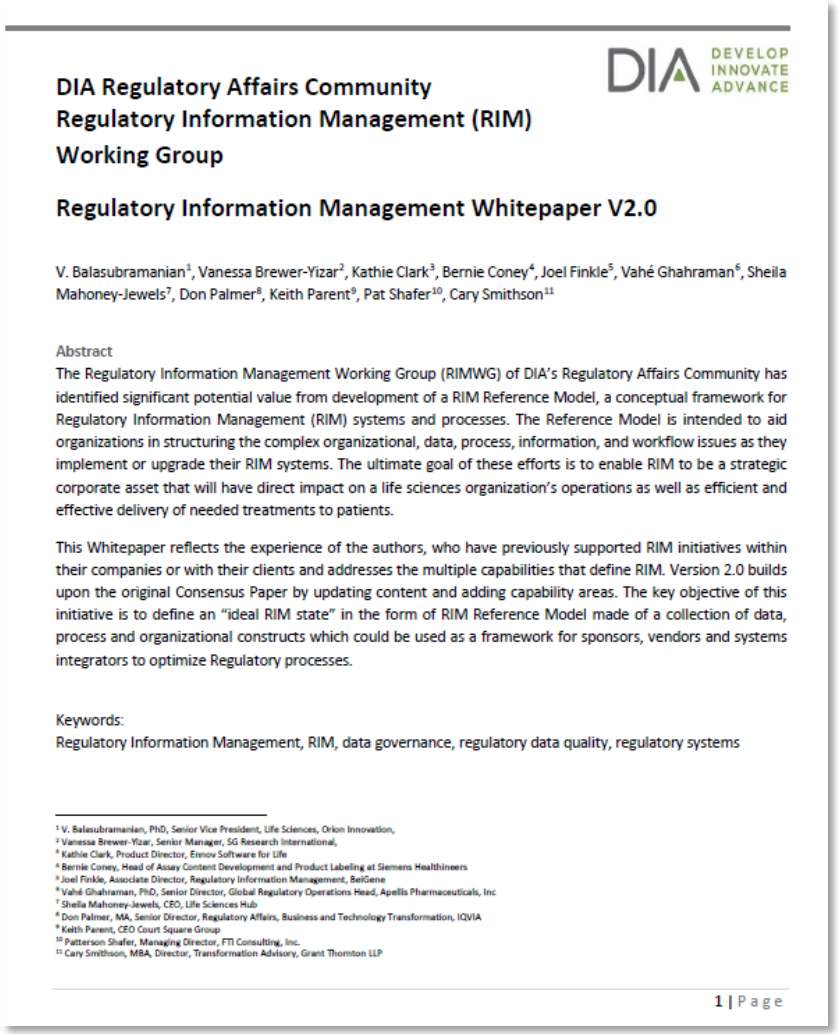
Volume
Number and type of submissions per year and market (including advisory); growth patterns

HA Responses
Number and type of health authority comments/rejections per year and market

On Time Submissions
Percentage on-time submissions

HA Approval Times
Time for approval (when explicit approval needed) by Health Authority

The Regulatory Information Management (RIM) White Paper



DIA DEVELOP INNOVATE ADVANCE

DIA Regulatory Affairs Community
Regulatory Information Management (RIM)
Working Group

Regulatory Information Management Whitepaper V2.0

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Abstract

The Regulatory Information Management Working Group (RIMWG) of DIA's Regulatory Affairs Community has identified significant potential value from development of a RIM Reference Model, a conceptual framework for Regulatory Information Management (RIM) systems and processes. The Reference Model is intended to aid organizations in structuring the complex organizational, data, process, information, and workflow issues as they implement or upgrade their RIM systems. The ultimate goal of these efforts is to enable RIM to be a strategic corporate asset that will have direct impact on a life sciences organization's operations as well as efficient and effective delivery of needed treatments to patients.

This Whitepaper reflects the experience of the authors, who have previously supported RIM initiatives within their companies or with their clients and addresses the multiple capabilities that define RIM. Version 2.0 builds upon the original Consensus Paper by updating content and adding capability areas. The key objective of this initiative is to define an "ideal RIM state" in the form of RIM Reference Model made of a collection of data, process and organizational constructs which could be used as a framework for sponsors, vendors and systems integrators to optimize Regulatory processes.

Keywords:
Regulatory Information Management, RIM, data governance, regulatory data quality, regulatory systems

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https://www.diaglobal.org/en/-/media/diaglobal/files/resources/tools-and-downloads/rim-reference-model.pdf

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