Note from the Commissioner

It has been a very busy first six months of 2018 for the PAAB. Both the board and the staff have been quite active.

The board has two code committees operating. One is looking at changing the definition of “advertising” for the PAAB Code of Advertising Acceptance. The other committee is looking at Real World Evidence data and how that can be used in advertising claims in accordance with the PAAB Code and if there are changes needed to the code.

The first six months of 2018 has seen a record volume of submissions combined with an unprecedented turnaround time efficiency by the PAAB staff. We have a great staff at the PAAB who work diligently to meet the needs of our clients. We have hired a reviewer, who will start in mid July, to replace a reviewer we lost late in 2017.

We have had 3 stage two complaints of which two were upheld. One of the APS had been reviewed and approved by the PAAB and the sponsor could continue use of the material until the expiry date.

We have finalized the agenda for the 2018 PAAB National Workshops to be held November 20 in Montreal and November 22 in Toronto. Watch for upcoming promotions coming from

CreateHealth IO, our events organizers. We have added some new content and some format changes with several external speakers. Should be a good one!

Sincerely,

Ray Chepesiuk

PAAB Commissioner

PAAB Stats

January 2018 through June 30, 2018

- Number of submissions: 4206
- Time to first response: an Average of 5.2 days.
- Time to revision response: Average 2 days

New PAAB Guidance Documents added to the website in 2018

No new guidance documents were added to the website during this quarter. But we are actively working on a couple of documents at the moment. If you'd like to know as soon as new documents are posted, follow us on Twitter @ThePAAB.

Breakdown of APS types in 2017

We've received feedback that it would be nice for the PAAB Newsletter to occasionally include a breakdown of the percentage of total HCP APS for each of the main categories of HCP targeted submissions. Here is the breakdown for 2017:

- Paper detail aid: 38%
- Service oriented items: 18%
- E-detail: 9%
- Internet: 9%
- Direct mail: 9%
- Opinion: 5%
- Journal ad: 4%
- Audio visual: 4%
- Slide presentations: 3%
- Social Media Marketing: 1%

Keep in mind that this breakdown is specifically for HCP pieces.

FAQ about the PAAB Code Change

We've been asked multiple times whether Section 6.6 (vii) from the previous version of the code no longer applies (or whether it was deleted by error during the code change). As a reminder, section 6.6(vii) had stated "Disease information materials which make no mention of treatment by name, class, or category AND are not linked to healthcare product advertising in any way, are exempt from PAAB preclearance". This code copy was removed by the multi-stakeholder committee simply to streamline the code. The copy was considered redundant given the other provisions listed in that part of the code (i.e. this does not signify a change in the breadth of the scope of preclearance).

PAAB Complaint Report April 1 - June 30

1. **ADVERTISER**: Tribute

COMPLAINANT: Pediapharm

SUBJECT: c18-01 Blexten Leave Behind and Booth Panel

PRECLEARANCE: Yes

ALLEGATIONS: 1. S2.1, 2.4. “As stated in our previous correspondence, the content of the Blexten promotional material is vague and does not reflect all the cautionary information from the Blexten product monograph that must be communicated to healthcare professionals. As a specific example, the proper administration of Blexten, as stated in the Health Canada approved product monograph, that "BLEXTEN TM once daily should be swallowed with water on an empty stomach to achieve optimal exposure to bilastine. The BLEXTEN TM tablet should be taken without food or grapefruit juice or other fruit juices, as these dietary compounds may decrease the effect of bilastine." This very important information needs to be clearly communicated to physicians so patients can be instructed on proper dosage and administration. In our opinion, the proper communication of dosage and administration of a new drug has always been a priority for the safety of the patient.”

2. S2.4, 2.10, 2.10.1: "Blexten: A new treatment for seasonal allergic rhinitis and chronic spontaneous urticaria” - This claim implies that Blexten can be given to all patients with seasonal allergic rhinitis and chronic spontaneous urticaria. This does not reflect the limitations of the product monograph and the approved indications by Health Canada”

3. "A study was performed to assess the effects of BLEXTEN and bilastine 40 mg on real time driving performance. .. By stating that bilastine 40 mg was studied "in real time driving performance" before the indication and the appropriate dosage are stated, this can mislead healthcare professionals to believe that bilastine 40 m is a roved b Health Canada, which is not the case.”

4. “Section on "Pharmacodynamic profile" The Pharmacodynamic section only emphasizes the positive features of Blexten and ignores the negative findings that should be included because of the significant impact on treatment such as:

Drug-Food Interactions

Plasma bilastine Cmax, AUC0-t, and AUC0-infvalues were approximately 33%. 17%. and 18% lower, respectively, for subjects receiving BLEXTEN TM following a high-fat breakfast compared to BLEXTENTM administered under fasted conditions. Plasma bilastine Cmax, AUC0-t, and AUC0-inf values were approximately 25%, 26%, and 25% lower, respectively, for subjects receiving BLEXTENTM following a low-fat breakfast compared to bilastine administered under fasted conditions. The Phase 3 clinical trials were conducted under fasting conditions to ensure clinically appropriate exposure to bilastine.

Grapefruit Juice

Concomitant administration of BLEXTENTM and grapefruit juice decreased bilastine bioavailability by approximately 30%. Concomitant administration of BLEXTENTM with other fruit juices may also

decrease bioavailability. The degree of bioavailability decrease may vary between producers and types of fruit juice. The mechanism for this interaction is an inhibition of OATPIA2, an uptake transporter for which bilastine is a substrate. Medicinal products that are substrates or inhibitors of OATPIA2, such as ritonavir or rifampicin, may likewise have the potential to decrease plasma concentrations of bilastine.

We also note that there is no mention of potential Drug-Drug Interactions, which can have a marked effect on bilastine plasma concentrations."

DECISION: 1. I agree with the allegation from Tribute. For a Healthcare Professional the Administration section in the Product Monograph contains important information relevant to optimal use of the product. In the case of Blexten HCPs should be aware of the administration section prior to prescribing or recommending the product. The claim "One dose, once daily" brings emphasis to the dosing and that should be balanced by instructions for proper use of the product to get optimal results. This requires fair balance. That can be done by adding a footnote in close proximity to the dosing claim to provide adequate fair balance.

2. I do not agree with this allegation because the PM indication is clearly stated in the APS in reasonable proximity.

3. I do not agree with this allegation because the information is complete and provided in a manner that does not mislead and is in accordance with the PAAB standard. The complainant has not provided proof of this being misleading.

4. I do not agree with Pediapharm because the presentation in the APS is consistent with current PAAB review practices if Tribute addresses allegation #1 about the proper administration.

SUMMARY and PENALTY: Therefore, I find allegation #1 to be substantive and worthy of correction. This can be addressed in future APS. PAAB will not renew the current APS when they expire. We encourage Tribute to address allegation #1 as soon as is possible to avoid the perception of misleading advertising. I thank Pediapharm to bringing this to the attention of the PAAB. I would like to hear a response from Tribute within 5 business days of electronic receipt of this ruling. If I receive no response as they indicated in their stage one behaviour, I will forward the complaint to Health Canada and ask them to investigate all of the allegations under the Food & Drugs Act. I did not see any evidence provided that patient safety has been compromised. If Pediapharm believes that to be true, they should contact Health Canada which is responsible for attending to those issues.

OUTCOME: Tribute agreed with the ruling.

2. **ADVERTISER**: Pediapharm

COMPLAINANT: Aralez

SUBJECT: C18-04 Pediapharm Rupall leave behind

PRECLEARANCE: Yes.

ALLEGATIONS: Verbatim from Aralez letter dated April 11, 2018. "The dosage information in this APS intentionally omits important information for appropriate patient selection that is found in the Dosing Considerations of your approved Product Monograph; we note that an earlier unapproved APS that was the subject of a complaint in June 2017 did include this important information under Dosage and Administration. We are surprised that a subsequent APS would be approved without this information.

Without this information, a prescriber will be unaware that use of Rupall in patients with any degree of renal or hepatic impairment is not recommended. This represents a departure from the body of common knowledge that health care providers can be expected to have developed due to familiarity with previously available antihistamines.

You assert that second generation antihistamines have a long history of renal and hepatic considerations, but there is no other antihistamine for which there is a blanket recommendation against use in patients with hepatic or renal impairment."

DECISION: I agree with the Pediapharm argument that the APS in question is consistent with current PAAB review practice regarding Fair Balance because these warnings are not emphasized in the product monograph (e.g. bolding, encasement in a box, usage of all caps, underlining). The fair balance provisions enable manufacturers to simply notify the HCP that warnings & precautions regarding patients with impaired kidney and liver function exist. The link to the complete product monograph is provided in case the physician is not aware of the identified issue and requires more information. These requirements are met in this APS as set out in the following guidance document:

http://code.paab.ca/resources/Guidance_on_Generating_the_Three_Base_Fair_Balance_Levels.pdf

SUMMARY and PENALTY: I find that there is no reason to change the ruling of the reviewer's decision regarding the fair balance issue raised by Aralez. The complaint is found to be not valid. In accordance with PAAB Code s1.7.E6, the PAAB will issue an invoice to Aralez in the amount of $500 for the registration fee of this complaint.

3. **ADVERTISER**: Volo Healthcare Inc.

COMPLAINANT: Biosyent

SUBJECT: C18-07 Optifer Alpha Detail Aid

PRECLEARANCE: No.

ALLEGATIONS:Page 1 (Exhibit A): The claim "and is better tolerated" is not specific to what the

comparison product is, or the statistical significance.

Page 2(Exhibit B): The claim “Fewer side effects” is not specific to what the comparison product is, or the statistical significance.

Page 3 (Exhibit C): i) The claim”Any patient who is at risk for iron deficiency should be recommended heme iron” is not referenced and seems to be an absolute statement not supported by any guidelines.

ii) The comparisontable is misleading as iron salts and PICs should not be grouped together as their mode of action sand efficacy are different. PICs do not require vitamin C. Iron salts do not need to be converted to Fe2. What is your reference that PICs are unaffected by foods? Further your “high bioavailability” with an ”X” to non-heme products suggest they are low bioavailablity. What is your reference for this?

Page 4 (Exhibit D): The claim “the incidence of side effects … will be virtually none”. You make this claim based on having a low dose. Please submit reference for your incidence of side effects.

DECISION: We make the assumption that the detail aid was directed to HCPs because of the Biosyent allegation of distribution. The PAAB agrees with the Biosyent allegations that the advertising is potentially misleading and does not comply with the standards in the PAAB Code. It should be disposed of and corrected material should be reviewed by the PAAB.

SUMMARY and PENALTY: 1. Stop distribution of said material to the representatives

2. Mandate to representatives to stop using said material immediately

3. To collect and destroy said material that they find in any HCP offices

OUTCOME: Volo agreed to the prescribed action.

Training and Events

National Workshops

We have finalized the agenda for the 2018 PAAB National Workshops to be held November 20 in Montreal and November 22 in Toronto. The day will cover a wide spectrum of topics including complaints on marketing materials, evidentiary standards, fair balance standards, patient information, social media, and artificial intelligence. As requested in prior event feedback, the day will include an advanced session covering some of the more complex nuances that occasionally arise during the review process. As also requested, it will include a question clinic. For the clinic, the room will be split into 5 parallel streams (each having a particular topic). This will enable attendees to ask questions about the stream's topic or simply listen-in to the responses provided to other attendees.

Important eFiles Submission News

Good News! Our eFiles Submission Form enhancements are complete!

With added information pop ups, this new form is designed to help you every step of the way. Enhanced programming to our eFiles Submission library provides new search and select options to simplify locating and uploading of multiple documents.

Check it out. We think you'll like what you see.

Please Note:

In consideration of submission trends and industry standards, the PAAB will amend the cut off time for same day processing of complete submissions.

Effective **August 13, 2018**, the cut off time for same day processing of complete eFile submissions will be one hour prior to the end of a business day. This change will apply to both, regular and summer business hours. Currently, summer business hours are 8:30-5:30pm Monday – Thursday and Friday 8:30 – 1:15pm, with eFiles submission cut off times of 5:30pm and 1:15pm respectively. As of **August 13,** the new eFiles cut off times will be **4:30pm Monday through Thursday and Friday at 12:15pm**. Efiles received at or after 4:30pm or 12:15pm, will be considered a next day submission.

PAAB staff training day – Aug 2, 2018

Please be advised the PAAB will be closed, Thursday August 2, 2018, for training purposes. Our office will reopen for business at 8:30 am Friday August 3. As this is a non-business day, August 2, will be excluded from eFiles timelines.

New PAAB Reviewer

We are welcoming a new reviewer to the PAAB team. Danielle Anthony is a Masters-prepared Registered Nurse with substantial work experience in pharmaceutical and OTC marketing.

The PAAB Code

To see the current edition of the PAAB Code, visit our website.

Our Mission

Vision: PAAB will be a world-class leader in supporting truthful advertising of health products.

Mission: To deliver pre-clearance review services that support trustworthy health product communications that comply with the Canadian regulatory framework

Values: Integrity, competency, credibility, independence, excellence, transparency

Social Media

PAAB LinkedIn Group

PAAB LinkedIn Page

PAAB Twitter

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