Note from the Commissioner

2017 was a busy and successful year for the PAAB. Due to our innovative mindset, we saw a lot of transformational change, and we met all our goals. We hope we are meeting your needs. The strategic plan was ratified at the AGM on April 21, 2017. The commissioner has developed an Operational plan, that looks to the future, based on that report. This will guide our activities. The board has reinstated the Executive Committee and the slate was elected at the September General Meeting. It will also act as an ad hoc Finance Committee to provide guidance for the Commissioner. We have developed a board work calendar based on the Strategic Plan.

As part of the strategic plan to improve communications, the Code Committee finalized an innovative digital, interactive format for the code and that was approved by the board on April 21, 2017, at the AGM. Implementation is January 1, 2018, and we have initiated communications plan to inform our clients. A staff committee worked with Innovasium to create and develop a new, innovative website that we launched January 2, 2017.

Internally we have revamped our financial accounting software to an innovative system to be able to integrate it into our customized E-file system. Internally we have implemented a modern HR software platform to improve our performance review system and enhance internal

communications.

The innovative ticketing/tagging system was implemented earlier this year and clients are starting to be familiar with it and we look forward to analyzing the data. We will continue to promote its proper use.

We had the annual bilateral meeting with Health Canada on April 18, 2017, during which we exchanged information and discuss issues of mutual concern. We also had a bilateral meeting with members of Health Canada regarding the advertising of self-care products as part of our attendance at the Health Canada consultation meeting on the modernization of self-care product regulations. The Commissioner participated in a Health Canada consultation meeting, by invitation, “Meeting the Needs of Canadians”. We discussed the merits of future HC initiatives.

The November training workshops held in Montreal and Toronto were a success. We had 450 registrants and all our speakers scored highly on the feedback forms we received. We continued our in-house training presentations at client companies. The Commissioner and Deputy Commissioner presented at external events on request. The Commissioner was a judge at the EyeforPharma Global Health Awards and the OPMA Skuy Awards.

We re-introduced the innovative PAAB Code Game supplied by 40Comets/Facilica after the workshops with changes based on feedback from clients. 153 registrants participated and had fun in a regulatory realm.

We have had a busy year on the review side and we handled the third largest review volume ever. The review efficiency was at its peak due to our amazing staff who continually find ways to create innovation in our systems. On the complaints side, we have had 5 stage two decisions this year with none of the material precleared by the PAAB and all five upheld. We had one stage three appeal completed in July with the commissioner’s ruling being upheld.

I hope that 2018 treats you well.

Sincerely,

Ray Chepesiuk

PAAB Commissioner

PAAB Stats

January 1 through December 31, 2017

- Number of submissions: 7408
- Time to first response: an Average of 5.6 days.
- Time to revision response: Average 2.1 days

New PAAB Guidance Documents added to the website in 2017

The following documents were added to the PAAB website:

How to present support program names

When program names can be interpreted as a claim, benefit or status for the sponsor's product, the program… Read more

[links to]:

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

Guidance on indication and fair balance font size

This document is meant to provide you with some guidance on acceptable font size and general type legibility… Read more

[links to]:

http://code.paab.ca/resources/Indication_and_Fair_Balance_Font_Guidance_-_Final_Draft_(1).pdf

The following documents were updated on the PAAB website:

Study Presentations Involving Dose Titration (an application of s3.1)

http://code.paab.ca/resources/Study_presentations_involving_dose_titration.pdfhttp://code.paab.ca/resources/Study_presentations_involving_dose_titration.pdf

The update elaborates on the level of emphasis required for the disclosure in Case 1a.

Guidance on eFiles Ticketing & Tagging

http://www.paab.ca/resources/Guidance_on_eFiles_Ticketing2.pdf

The update elaborates on instructions relating to the use of the tagging system.

Guidance on Advertising for Drugs with Notice of Compliance with Conditions (NOC/c)

http://code.paab.ca/resources/Guidance_on_Advertising_for_Drugs_with_Notice_of_Compliance_with_Conditions_(NOCc)._September_2017.pdf

The update includes the addition of guidance for patient information when a product has a combination of related NOC and NOC/c indications.

If you'd like to know as soon as new documents are posted, follow us on Twitter @ThePAAB.

Update Regarding Risk Minimization Tools

Here's a quick reminder that near the end of August 2017, we've added two new items to the"Disclosure Type" section of the PAAB submission form. The new disclosure types are "**Product Branded Risk Management Tool"** and "**Unbranded Risk Management Tool"**. This will help streamline the submission registration process for our clients and for our file coordinators as risk management tools will now automatically be assigned the appropriate turnaround times. To avoid re-processing delays, only select a risk management tool disclosure type for materials which are part of a Health Canada mandated or Global mandated risk management plan or program. For more information regarding Risk Management Tools visit:

http://code.paab.ca/resources/Guidance_on_Risk_Managment_Tools_(September_2016typo_fixed)_(1).pdf

New Code and Website Format

As a reminder, the new Code and Website formats are up and running. All PAAB letters will cite the PAAB code sections from the new code format. As some code sections were

repositioned to improve the code flow, you may notice changes in some of the code sections referred to in our letters. This has no impact on what is (or is not) acceptable. You can directly access the PAAB Code App at the following URL: http://code.paab.ca . Alternatively, the code App may be accessed through our website at www.paab.ca. On the website, the code is accompanied by a letter describing how this innovation will benefit you. The letter also identifies which code sections have been repositioned. The letter can also be accessed at the following URL: http://www.paab.ca/resources/Letter_from_commissioner.pdf

You will notice that the format of the PAAB website has also been improved. While the new code format was designed to help you get more out of the PAAB code, the new website format was designed to help you get more out of all the other important information on the website. One of the key website features includes the ability to search and filter for documents on the website such as guidance documents and review tips. To help you keep up to date, you are now able to identify any newly posted documents as soon as you go to the resource page. They are listed at the top of the resource page accompanied by the icon “new”. This is just another step towards realizing our vision of being a world-class leader in supporting truthful advertising of health products.

PAAB Complaint Report 2017

Stage Two Decisions January 1 to December 31, 2017

1. ADVERTISER: Merck
COMPLAINANT: Amgen
SUBJECT: c16-09 Interview Article in “Biotechnology Focus” promoting Brenzys
PRECLEARANCE: No

ALLEGATIONS: The Interview does not fall under any of the prescribed categories of exemptions from the Code.

Amgen's position is that the Interview was not independently conducted by Biotechnology Focus' perspective, and so the exception set out in Section 6.6(i) of the Code would not apply. Merck's involvement in the Interview is not limited to purchase

or sponsorship of the distribution. None of the other Section 6.6 exemptions are applicable to the Interview. ·

Sections 1.1 and 2

The Interview is a promotional piece that is subject to PAAB 's oversight as its intended audience is healthcare professionals.

Section 2.1 and 2.3
the Interview states that there are no safety or efficacy differences among patients who transitioned to BRENZYS™ from ENBREL®. Indeed, in advocating that BRENZYS™ receive preferential formulary listing as a biosimilar, Mr. Mader makes the following statement: "I think with BrenzysTM, we've shown that our product is as efficacious and as safe as the originator product".

The Interview emphasizes only the positive features of BRENZYS™, and makes no mention of any negative findings or safety issues. As discussed above, the efficacy and safety claims that appear throughout the Interview are not balanced by any discussion of negative findings. In response to the interview question "What are the strongest concerns you've heard about biosimilars?", Mr. Mader responded by lauding Merck's commitment to patient safety and stating that there is no difference in terms of safety between BRENZYS™ and ENBREL®.

Sections 5.10, 5.11 and 5.12

Section 5.10 of the Code requires that any claims making direct or indirect therapeutic comparisons between drug products must not mislead and be supported by reliable current clinical data. As described above in this letter, Amgen is of the position that Merck's claims in the Interview that the safety and efficacy of BRENZYS™ support transitioning patients from ENBREL® to BRENZYS™ is not supported by any peer reviewed, published and Health Canada-approved data. Nor is there any such data in the product monograph to support Merck's claim that there are fewer injection site reactions associated with BRENZYS™ as compared to ENBREL®.

Section 5.11 and 5.12 of the Code also require that claims must be made in the context of the study conclusions and that in no circumstances would extrapolation of a claim beyond the actual conditions of the supporting study be acceptable. The data

used by Merck to make the abovementioned statement regarding fewer injection site reactions is based on a study published in the journal Annals of the Rheumatic Diseases, 1 Emery P, et al. Ann Rheum Dis 2015;0: 1-7. doi: 10.1 136/annrheumdis-2015-207588 which was analyzed in the European Medicines Agency's ("EMA") 2015 Assessment report of the EMA Marketing Authorization application for BENEPALI™ (the brand name that BRENZYS™ is marketed under in the European Union).2 The EMA concluded that the data comparing injection site reactions occurring after administration of ENBREL® with corresponding reactions related to BENEPALI™ had no clinical significance.

DECISION: Health Canada was consulted and confirmed that they considered the item to be advertising under the Food and Drugs Act and that there were alleged misleading statements in violation of section 9 of the Act.

The interview was with a Merck employee who could have tempered his comments and also Merck had a chance for review of the APS. PAAB preclearance review is designed to avoid violations of the PAAB Code.

I agree with Amgen that there are breaches of:
Code Sections 1, 2.1, 3.1, 3.5, 5.10, 5.11 and 5.12.

Summary and Penalty

This APS should have been submitted to the PAAB for review within the PAAB Code. There are multiple violations of the PAAB Code.

OUTCOME: Merck filed a PAAB Code s9.7 Stage Three Appeal based on their belief that the APS did not fall under the scope of advertising. The Panel upheld the commissioner's ruling.

2. ADVERTISER: Merck
COMPLAINANT: A Group of four companies, Roche, Janssen, AbbVie, Takeda
SUBJECT: c17-01 Editorial Advertising "The Rise of Biosimilars" appearing in "Benefits Canada" December 2016.
PRECLEARANCE: No

ALLEGATIONS: verbatim from the complainants:

- The Report falls within the scope of the Code, and none of the exemptions set out under section 6.6 of the Code apply to the Report.

- The Report contravenes section 2.3 of the Code in its discussion of the NOR-SWITCH clinical study.

- The Report contravenes section 2.4 of the Code, as it advocates for the transitioning of stable patients to an alternative therapy for purely financial reasons, without supporting medical justification.

- The Report contravenes section 2.6 of the Code in making sweeping and unqualified statements on the safety and efficacy of biosimilars.

- The Report contravenes section 3.1 of the Code in making multiple claims which:

o may be inferred as relating to BRENZYS (a recently approved product and a biosimilar of ENBREL® which Merck markets in collaboration with Samsung Bioepsis Co.)

o go beyond the scope of the terms of marketing approval for BRENZYS (BRENZYS is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults, and for reducing signs and symptoms of active ankylosing spondylitis);

o are incompatible with Health Canada's official statements on biosimilars; and

o are not supported by proper references or evidence.

- The Report contravenes sections 3.7 and 5 of the Code, as it draws improper conclusions on biosimilars as a class from limited evidence available for

biosimilars of REMICADE®, namely INFLECTRA®.

- The Report contravenes section 2.1 of the Code, in mischaracterizing the way in which Health Canada will “extrapolate” indications for biosimilars.

- The Report constitutes a violation of the Food and Drug Act restrictions on Direct-to-Consumer advertising by virtue of ready access in the public domain through publication on the non-gated Benefits Canada website. Based on prior Health Canada ruling on parallel issues (Rx&D complaint to PAAB regarding advertisements sponsored by the Canadian Generic Pharmaceutical Association (CGPA) (attached), we are also referring the matter of violation respecting Direct-to-Consumer advertising directly to Health Canada for consideration in parallel.

DECISION: PAAB will rule on the nature of and the distribution of the published Report because there appears to be intent of distribution by email to a target audience that is known to include health professionals who make decisions on what drugs doctors are encouraged to prescribe within various drug plans. PAAB has previously stated in response to questions that paid articles in Benefits Canada could be considered to be advertising if distributed to healthcare professionals. To my knowledge, the PAAB has not had complaints about Benefits Canada articles in a good number of years.

The DTC website version is being referred to Health Canada as DTC.

The Report is considered to be advertising because it was a paid insertion in Benefits Canada magazine, Merck had review privilege prior to publication and the content serves to promote Brenzys, a Merck biosimilar product. It would fall under s7.5 of the PAAB Code for review purposes as it is editorial in nature and Merck has stated they did not seek to promote Brenzys specifically.

Therefore, there is a violation of S1.1 of the PAAB Code of Advertising Acceptance in that Merck did not submit this for PAAB review.

The Complainants also make allegations about the content and they state “Rather, the Report promotes Merck’s biosimilar product Brenzys and includes a plethora of

misleading and inaccurate statements as detailed in the Stage 1 complaint letter dated February 10, 2017."

We did not see a "plethora of misleading and inaccurate statements" in the PAAB informal review. There appear to be violations of s2.4 and 2.6 because of statements such as "They're safe." In an absolute manner. There appears to be some violation of s3.1 because of statements supported by inadequate evidence such as abstracts or statements that may go beyond the Marketing Authorization for individual products. That would be captured in a formal PAAB review and that is not the purpose of this complaint ruling.

Summary and Penalty
The PAAB has ruled that the item is an advertising/promotional system subject to review and there are alleged violations of safety and efficacy statement provisions in the PAAB code.

OUTCOME: The website was corrected by Merck. Merck registered a Code s9.7 Stage Three Appeal which was withdrawn by Merck.

3. **ADVERTISER**: Allergan
COMPLAINANT: Lundbeck
SUBJECT: c17-04 Fetzima Detail Aid
PRECLEARANCE: No
ALLEGATIONS: See decision
DECISION: 1. The claim "Unique" – we agree with Lundbeck that Allergan has not proven an exclusive "only" claim based on the reference data cited in the APS. This claim was previously rejected by a PAAB reviewer in another APS.
2. "The ratio of serotonin to norepinephrine reuptake inhibition in select SNRIs" is based on a review article – Unacceptable to the PAAB Code s3.1.1 and 5.10.2.
3. "With a higher ratio of norepinephrine to serotonin reuptake inhibition, Fetzima significantly improved patient motivation and energy". This statement links non-clinical parameters to clinical benefits. This contravenes PAAB code s4.1.1, 3.1.4, 2.6.2.
4. "Effective anti-depressant action. Fetzima significantly improved MDD symptoms vs. placebo at all therapeutic doses." This claim is not acceptable to the PAAB code 3.1.5. It is too broad and is not reflective of the results of one study. It should be deleted.

5. "MADRS mean total score improvement in depressive symptoms at Week 8." The corresponding bar graph below this statement is missing the study parameters for the data quoted. This violates 4.2.1 of the PAAB code.

6. "Introducing Fetzima. The only SNRI that offers a 2- fold greater selectivity for norepinephrine versus serotonin reuptake inhibition". It is referenced to a review article, which is a violation of 3.1.1 of the PAAB Code. Furthermore, the wording is not completely reflective of the wording in the product monograph, which is: Levomilnacipran inhibits the uptake of both NE and 5-HT in-vitro and in-vivo; preferentially inhibiting uptake of NE over 5-HT by approximately 2-fold. This is a violation of section 3.1 of the PAAB code.

7. PAAB has no objection to adding representative contact info if it does not alter the context of the APS approved by the PAAB.

8. With respect to the visual on the front of the piece and the headline "Find the spark", these are both in violation of section 2.1, 2.3, 2.6 and 5.16, as they are implying that Fetzima will restore "the spark" (a superlative, absolute claim) back into MDD patients. This is not supported by the product monograph. This was previously rejected by the PAAB.

9. Due to timing issues of first marketing, PAAB does not agree with the allegation “Additionally, the claim of "Introducing Fetzima" is only permissible for one year after the product has received NOC in Canada. According to the Health Canada NOC database, the product was first approved by Actavis on May 8th, 2015; therefore, "introducing" would need to be removed from the APS as this contravenes section 3.1 of the code.”

OUTCOME: File was referred to Health Canada because of non-compliance with previous PAAB rulings. Pending Health Canada investigation and decision.

4. **ADVERTISER**: Bayer

COMPLAINANT: Novartis

SUBJECT: c17-05 Now I Know website and Leaflet in support of Eyelea

PRECLEARANCE: No

ALLEGATIONS: PAAB should have reviewed website and multiple misleading claims alleged.

DECISION: The leaflet in question falls into the PAAB Code scope and should be submitted for review. The website is in the DTCI realm as intended by Bayer and, thus, does not fit in the scope of the PAAB Code. The Novartis allegations of “promotional, misleading, deceptive, inaccurate and incomplete” should be directed to

Health Canada.

With respect to the confusing practice of creating a DTCIRx communication and then distributing messages to health professionals to encourage distribution to patients, Novartis should direct that issue to Innovative Medicines Canada for review by the Marketing Ethics Committee.

I note Bayer has stated that they have discontinued distribution of the leaflet. Bayer should submit similar material to the PAAB in future. No other penalty is issued by the PAAB.

In future for APS of this nature, if the website has been reviewed by ASC, PAAB will ask for the inclusion of a prominent disclaimer on the leaflet saying the website was not reviewed and approved by the PAAB.

OUTCOME: Agreement with the ruling.

5. **ADVERTISER**: Pediapharm

COMPLAINANT: Aralez

SUBJECT: c17-06 Rupall Detail Aid

PRECLEARANCE: No

ALLEGATIONS: See decision

DECISION: The preclearance review service was not used by Pediapharm and that is a violation of the PAAB code. In addition, there are several significant violations of the PAAB Code. Additional violations of the PAAB Code may have been identified if the PAAB was able to evaluate the support material for some of the claims. These were not provided.

In particular:

1. Innovative Medicines Canada has no direct bearing on whether an APS is in contravention of the PAAB Code. Pediapharm is advised to read the “Overview of Drug Advertising” to be found on the Health Canada website for the relevance of the PAAB Code of Advertising Acceptance s1.1. We agree with Aralez.

2. **Aralez Allegation**

"Non-sedating and long-term safety profile" Section 2.6.1The Code does not accept statements that claim directly, or indirectly, 100 percent clinical efficacy or safety.

Section 4.3: Data presentations which are misleading or ambiguous, or which distort the original meaning or interpretation, either directly or by implication, are in violation of the PAAB Code. This copy indirectly implies 100% non- sedating and long-term safety.

This copy is misleading based on the TMA which states in the Adverse Drug Reaction Overview section "The most common adverse reactions reported with Rupall 10 mg were somnolence, headache...."

We agree with Aralez that this is a significant violation of the PAAB code and has the potential to mislead. S2.4 is also violated regarding the lack of caution.

3. The Aralez Allegation:"The allergy medication with a unique dual action of antihistamine and anti· platelet activating factor " Section 2.6.2: The advertiser may make properly supported absolute statements when describing product properties (e.g. pharmacology, actions, kinetics,etc.) if these are presented or grouped separately from the clinical claims section; this avoids any extrapolation of laboratory superiority to imply clinical efficacy or advantage. We object to the position of these non- clinical product properties beside clinical claims of efficacy. There is no disclaimer attached to these product properties of "clinical significance unknown ".

We agree with Aralez that the visual is potentially misleading because of the direct link of clinical and non-clinical parameters. These clinical claims are not supported by the Product Monograph.

4. Other Aralez Allegations

The Commissioner was unable to make an evaluation on the other allegations because the relevant support material was not provided. These can be evaluated during a PAAB preclearance review.

Summary and Penalty

The APS in question is clearly in violation of the PAAB Code and would have benefited from a PAAB preclearance review. I request Pediapharm to withdraw this APS from the marketplace and stop further distribution. I would like to see an action plan and messages directed at Pediapharm staff to withdraw this APS and agreement to stop further distribution.

OUTCOME: Pediapharm agreed to comply with the PAAB ruling.

Training and Events

PAAB Code Game Winners

Although everyone who played the PAAB code is a winner, here are the participants who got the top scores:

1. Alison Sinclair – Won 2 tickets to the OPMA Skuy Awards Feb 2018
2. Harshani De Silva – Won 1 ticket to the Skuy Awards
3. Brenda Gryfe – Won 1 ticket to the Skuy Awards
4. Dave Makerewich – Won bragging rights
5. Chris Czaniecki – Won bragging rights

Thank you to all who played the game and I hope you had a great fun and educational experience. We had 153 registrants with a 40% completion rate.

We thank Yves Bordua of 42comets for providing the Facilica powered game. You can get more info about the gaming experience from www.42comets.com

Are you making the most of the PAAB's innovative tagging system?

The tagging system was created to enable our clients to efficiently provide feedback and thus help us enhance the PAAB preclearance mechanism. There is a wide spectrum of standardized tags ranging from review issues such as perceived inconsistencies to perceived opportunities

for improving the code and/or guidance documents.

Once created, the tag remains on record and cannot be deleted by any PAAB staff. As per client request, **client tags are NOT visible to the reviewer.**

What's the value?

- Utilizing the tagging system empowers our clients to express their feedback and get it documented (exactly as expressed) directly into a single centralized record.
- It enables the PAAB management team to detect trends which can lead to the expedient implementation of improvements to our processes, procedures, and practices (e.g. training & development).
- It can assist in determining areas of focus during audits of the preclearance system.

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

PAAB LinkedIn Group

PAAB LinkedIn Page

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