PAAB COMPLAINT REPORT 2015 Total

During the period of January 1, 2015 to December 31, 2015, the PAAB Commissioner processed 6 Stage 2 complaints.

In addition, PAAB has continued to regularly monitor journals, the Internet, and receive direct-mail/detail aid materials collected by health professionals as part of its monitoring program. When Code violations are discovered, PAAB sends a letter to the advertiser seeking their cooperation to meet the requirements of the Code. When appropriate, PAAB will notify the advertiser's trade association and/or Health Canada for their assessment of additional penalties.

STAGE TWO DECISIONS

File #C15-02
ADVERTISER: Pfizer

COMPLAINANT: Sanofi

SUBJECT: Epipen APS various

PRECLEARANCE: Yes

ALLEGATIONS: Sanofi alleges that "The Pfizer Canada 2 Steps Campaign provides misleading and incomplete information in violation of the PAAB Code." This is "in various advertisings to health care professionals and the general public (including on television) and paper materials is based on the tag line and premise that EpiPen only requires two simple steps". Sanofi states "The reference to two steps gives the public the general impression that the use of an EpiPen auto-injector in case of a severe anaphylactic reaction solely requires two actions".

DECISION: A check of our records indicates that the PAAB has not reviewed and approved the television APS nor has reviewed and approved the tag line mentioned in the Sanofi allegations. Therefore this ruling is restricted to the multiple APS to Health Care Professionals and Consumers reviewed by the PAAB since 2008 when this "Two Steps" campaign was first reviewed and approved.

I also note that the Sanofi letter does not include any specific PAAB Code of Advertising Acceptance sections as being violated.

I reject the Sanofi stage two allegations for the following reasons:

1. No PAAB Code section has been identified making it difficult to relate how the PAAB code has been violated.
2. Pfizer has stated that the depiction of the method of use of Epipen is consistent with the Health Canada approved package labeling regarding the use of 1 and 2 in graphic format.

3. The depiction of the method of use in advertising approved by the PAAB is consistent with the depiction in the Health Canada approved Product Monograph which has no quantitative statement about the number of steps. The PM lists the actions one must take to use the product properly.

4. While multiple actions are shown in the PM, the labeling has grouped them into two numbered steps for ease of presentation and understanding by the user.
5. I believe that Pfizer has attempted to simplify the instructions , similar in manner to the package label, to help people understand the instructions in an easier manner. The phrase “Blue to the sky, Orange to the thigh” reflects this effort.The graphic presentation supports this effort.
6. The PAAB approved materials have been in circulation since 2008 and we are not aware of any other complaints or safety issues related to improper use occurring as a result of the promotional materials.

OUTCOME: The complaint is rejected and therefore we require no further action by Pfizer to address the allegations. In accordance with PAAB Code section 9.4.6 the PAAB will send an invoice to Sanofi for recovery of the registration fee of $500 for this rejected complaint.

File #C15-03
ADVERTISER: GSK

COMPLAINANT: Pfizer

SUBJECT: VotrientAPS

PRECLEARANCE: Yes

ALLEGATIONS: Excerpted: “Pfizer understands that the above-mentioned APS has gone through a PAAB review; however Pfizer is of the view that the content of the APS is not compliant with sections 2.3, 4.2, 5.2, 5.5, 5.6, 5.7, 5.9, 5.10 and 5.11 of the PAAB Code. It contains misleading claims that are based on inadequate supporting material and statistics that are not presented in a clear and transparent manner.”

#1 Recommendation by Pfizer: Change the language in the headline of the APS to be more transparent and accurately reflect Votrient's efficacy as "non-inferior to sunitinib in the ITT population only".

#2 Recommendation by Pfizer : Add more precision to the statement about non-inferiority not being met in the per protocol I population including the numerical values for this analysis 8.4 vs 10.2 months to give equal representation to ITI and PP analysis.

#3 Recommendation by Pfizer: Add the omitted study design details in all future material citing COMPARZ:

- **assessment biases for progression and adverse events**
- **the fact that COMPARZ was amended to include two different studies**
- **25% NI margin translates into a -2 month PFS timeframe.**

DECISION: I do not wholly agree with the Pfizer allegation "It contains misleading claims that are based on inadequate supporting material and statistics that are not presented in a clear and transparent manner. " Based on the above analysis and decisions I do not see a need for GSK to withdraw the current APS as approved by the PAAB and GSK will be required to add additional footnotes in future APS to help improve the context of the claim. GSK should share this ruling with their advertising agency. As a note to Pfizer and as an observation to GSK, our records show that GSK made written comments to the reviewer during the review process that the submission file review was inconsistent with other PAAB reviews in that it was too rigorous. This review was no exception to all PAAB reviews. Scientific rigour is looked for and context of claim is always important to the reader

OUTCOME: Agreement by both parties to close case.

File #C15-04
ADVERTISER: Odan

COMPLAINANT: BioSyent

SUBJECT: promotional systems for Odan Polysaccharide Iron Complex.

PRECLEARANCE**:** No.

ALLEGATIONS: In APS distributed to health professionals Odan claimed that theirNatural Health product "is a generic iron complex duly approved by Health Canada containing 150 mg of iron and is therefore, from a therapeutic perspective, comparable to BioSyent's FeraMax 150 mg product.". PAAB received clarification from Health Canada about the claim of "generic equivalence" which stated "Although Health Canada does have guidelines about bioequivalence for products regulated under the Food and Drug Regulations, these do not apply to NHPs. There are no patents for NHPs and therefore no generics and no bioequivalence policy. However, comparative claims (eg: equivalent efficacy, same duration of action, etc.) are permissible and should meet the requirements set out in the Therapeutic Comparative Advertising Directive and Guidance Document."

DECISION: Agree with BioSyent that Odan's claims for generic equivalence are false and misleading because there are no generic NHP's and Odan has provided no scientific evidence for bioequivalence to Feramax 150 mg.

OUTCOME: Both parties agreed with the decision.

File #C15-07
ADVERTISER: Medical Futures Inc.

COMPLAINANT: BioSyent

SUBJECT: 3 promotional detail aids distributed to pharmacist

PRECLEARANCE: No.

ALLEGATIONS: Alleged misleading claims regarding "optimal iron" and alleged potentially misleading comparative claims vs Feramax.

DECISION: Ruled in favour of BioSyent allegations. MFI to cease and desist the alleged claims and recall material if distributed to health professionals.

OUTCOME: Both parties agreed with the decision.

File #C15-08
ADVERTISER: Biogen

COMPLAINANT: Serono

SUBJECT: Biogen APS

PRECLEARANCE: No.

ALLEGATIONS: Verbatim from the EMD Serono letter of June 8, 2015

"Promotional Item TF-CAN-01 10-E (see Appendices):

> We acknowledge Biogen's response that this piece is no longer in use. However, we maintain our objection to the claims made in this piece and are concerned that future pieces will simply be developed to contain similar content (as was seen in the promotional fax sent out on May 4, 2015) and then subsequently retired upon complaint. In fact, this appears to be exactly what occurred following our May 2014 complaint on TECFIDERA materials - Biogen agreed to retire the piece, but simply created a new TECFIDERA piece using the same or similar claims. Given this pattern of conduct, we request assurance from Biogen that all future pieces will be submitted for PAAB review to address

concerns such as those cited in our letter dated May 27, 2014, as well as our letter dated May 29, 2015, some of which are outlined below.

Promotional Item TF-CAN-01 10-E (see Appendices):

We do not agree with the explanations brought forth by Biogen in their response letter dated June 24, 2015. To summarize our main concerns:

- The headline 'High Efficacy'-While we recognize that 'high' is subjective in nature, we believe that a 49% RR or 38% RR does not convey 'high efficacy' and is potentially misleading. (PAAB s2.1, 2.3).
- 67% reduction in annualized relapse rate claim -The claim '67% reduction' is based on a sub-group analysis in treatment-naive patients which is not supported by the
  TECFIDERA Terms of Marketing Authorization (TMA) and therefore in violation of PAAB s3.1. As a general comment, all 'reduction' claims should specify 'relative reduction' to be accurate and clear. (PAAB 4.2) In addition, even in selecting sub-group data, as indicated in our letter on May 2014 complaint, only a select data point was included, while other sub-groups that demonstrated either a decrease or absence of treatment effect on relapses and disability progression across the phase Ill trials (e.g. female trial participants, previously treated trial participants, trial participants older than 40, trial participants with EDSS 2.0) were omitted, and thus we assert that Biogen is "cherry- picking" data.
- 72% reduction in mean number of T1 lesions claim -As stated in Biogen's response, this claim was based on a 'tertiary endpoint' in the Clinical Study Report and referenced as data-on-file (DoF). We understand DoF may be acceptable to PAAB as long as the data does not contradict the TMA. In this case, the claim over-states the efficacy data in the TMA (Table 4), which only presents a 57% relative reduction over 2-years. (PAAB s3.1, 3.1.2).
- Convenience- While we recognize (in current PAAB approved ads) that 'convenience' is often restricted to the oral dosing aspect of the therapy, it is potentially misleading to extrapolate this to the monitoring requirements. As cited in the TECFIDERA TMA (page 8), several tests are required over a period of time. The placement as a heading above 'monitoring' is potentially misleading.
- Generally well-tolerated-We believe that it is potentially misleading to claim 'generally well tolerated' without presenting any incidences of adverse events or discontinuation rates. This does not reflect an attitude of caution (PAAB s2.4, 3.5), especially in light of the important safety information update issued by Health Canada on February 6, 2015, communicating that the risk of Progressive Multifocal Leukoencephalopathy (PML) is being added to the Tecfidera Canadian Product Monograph.

2.

- Favorable safety profile-The bullet points that follow 'Favorable safety

profile' are non- clinical features and misleadingly suggest clinical benefits from non-clinical parameters. (PAAB s3.1.4, 2.1).

As noted above, we do not agree with Biogen's response to our concerns and are very concerned about the marketing practices that Biogen is utilizing. We look forward to PAAB's assessment of the complaint under s. 9.6.1 and appreciate your time in looking into this matter. »

DECISION: The ads in question contain several code infractions, many of which are repeated throughout the piece and many of which are described in detail within the EMD Serono letter. Some of the most flagrant code Infractions I've noted include:

- Failure to reflect past study findings in claims and data presentations from clinical trials. (PAAB s2.3)
- Contextually according clinical significance to non-clinical features where no such significance has been substantiated. (PAAB s2.6.2 & 3.1.4)
- Employing overtly superlative claims which have not been substantiated. (PAAB s5.16)
- Presentation of unacceptable data. (PAAB s3.1.2)
- Employing absolute and overly broad claims which are unsubstantiated. (PAAB s2.1 & 2.6)

These infractions could have been avoided through use of the PAAB preclearance process.

Summary and Penalty

Biogen should cease distributing the promotional materials in question and materials with similar content alleged to be in violation of the PAAB Code of Advertising Acceptance. Biogen should recall and retrieve such material from the marketplace. We invite Biogen to preclear all APS through the PAAB.

Biogen should inform me in writing no later than Wednesday July 22, 2015 that they will comply with this ruling and give an action plan with dates of how they will remove the violative material from the marketplace.If Biogen does not agree to the above request, I will transfer this complaint to Health Canada and request enforcement where appropriate.

OUTCOME: Agreed.

File #C15-12
ADVERTISER: Novartis

COMPLAINANT: Biogen

SUBJECT: Internal training document that was used as product promotion by a sales representative

PRECLEARANCE: No.

ALLEGATIONS: *As you will note from the attached correspondence, the parties have attempted to resolve the matter through intercompany dialogue and have been unable to do so. The Novartis response is inadequate, as Novartis repeats in its December 7, 2015 letter (the "Stage 1 Response") that the Document was "not advertising", that its contents were "accurate" whether advertising or not, and that in any event its response has been "adequate" with the issues raised by Biogen having been addressed already. All three Novartis contentions are incorrect.*

While Novartis evidently drafted the document so as to give the appearance that it was not promotional (going so far as to include a disclaimer that the document was "for internal training use only"), in Biogen's view the document was clearly intended, notwithstanding the "disclaimer", to be used in a promotional manner, and was in fact so used. The clearest proof that the document was used in a promotional manner is the fact that Biogen became aware of its existence when it was forwarded to Biogen by a Canadian physician who had been e-mailed the document unsolicited. The fact that the contents of the document contain numerous comparisons with the Biogen product (to its disadvantage) make nonsense of the claim that the Document was intended to be purely "reactive" to "unsolicited" questions. Even assuming for the sake of argument that sending the Document to a Canadian physician was a 'singular mistake' (of which there is no proof), it is evident that the Document was always intended for promotional purposes.

The Document is beset with inaccuracies, the details of which, and the relevant PAAB Code violations, are outlined in our November 25, 2015 letter (the "Stage 1 Complaint"). We repeat and rely on these allegations for the purposes of this Stage 2 Complaint.

There is a serious issue in contention here - namely, whether a manufacturer may, by using the right disclaimers, disseminate promotional materials to Physicians that make inaccurate statements and comparisons with competing products concerning very significant (and potentially life-threatening) adverse drug effects. The absence of any demonstrable explanation as to how Novartis allowed an inaccurate, promotional document to be proactively advertised to the Canadian Medical Profession, and the absence of recognition by Novartis of the significant Code breaches, leads us to conclude that such matters now require a serious response and genuine attempt at remediation, as outlined in our Stage 1 Complaint. We are now requesting your judgment on the matter.

DECISION: I commend both parties for trying to resolve this through intercompany dialogue in the spirit of self-regulation. I do regret that after such a lengthy period of discussion it has come to the PAAB for resolution.

There are two PAAB Code related issues concerning the document in question raised by Biogen.

The first one is the allegation that the distribution of this document was “advertising”. Novartis contends it was a document intended to be used as internal training and is marked as such. Internal training documents are not within the scope of the PAAB Code because they would not be considered advertising in their pristine existence. Biogen has provided the document and has stated that it was sent unsolicited by email to a Canadian physician. Novartis has not denied the claim of distribution to one physician.The content of the document is related to the two companies’ competing products. There appears to be no evidence of further distribution provided by Biogen. We look for guidance from PAAB Code s11.1 which **defines “advertising” as any paid message communicated by Canadian media with the intent to influence the choice, opinion or behaviour of those addressed by commercial messages. Distribution of any unsolicited material about a pharmaceutical product is deemed to be advertising if the information or its distribution serves to promote the sale of that product either directly or indirectly.**

Therefore, the act of distribution by a Novartis employee appears to be an act of advertising, albeit to one Canadian physician. Biogen has provided no evidence that Novartis directed the employee to send this to that physician and there is no evidence that there was intent of wider distribution.

The second code related issue is the Biogen allegation that the document contains inaccuracies disparaging to their product and this would be related to several provisions in S2 and S5 of the Code. Indeed the PAAB preclearance review mechanism is designed to prevent inaccuracies and disparaging comparisons. I have asked PAAB review staff to look at the document and they tell me there are inaccurate comparisons that would breach several provisions of the PAAB Code. PAAB looks for evidence to support claims. Sometimes opinion gets in the way of a supportable claim.
Novartis states in their stage one letter “This Document was distributed to a limited number of Novartis Medical associates following internal content approvals and training by Novartis personnel using standard operating procedures. Further, following receipt of your complaint, we have also reinforced our communication with internal associates.” This is not clear to me that Novartis has corrected the inaccuracies in the document that was intended for training Novartis personnel to communicate to health professionals.

OUTCOME: Agreed.

File #C15-07
ADVERTISER:

COMPLAINANT:

SUBJECT:

PRECLEARANCE:

ALLEGATIONS:

DECISION:

OUTCOME

File #C15-07

File #C15-07
ADVERTISER:

COMPLAINANT:

SUBJECT:

PRECLEARANCE:

ALLEGATIONS:

DECISION:

OUTCOME

File #C15-07
ADVERTISER: Medical Futures Inc.

COMPLAINANT: BioSyent

SUBJECT: 3 promotional detail aids distributed to pharmacist

PRECLEARANCE**:** No.

ALLEGATIONS: Alleged misleading claims regarding "optimal iron" and alleged potentially misleading comparative claims vs Feramax.

DECISION: Ruled in favour of BioSyent allegations. MFI to cease and desist the alleged claims and recall material if distributed to health professionals.

OUTCOME: Both parties agreed with the decision.