

A 6-Year Retrospective Analysis of Cardiovascular Safety Consultations in Large Pharma

Roger M. Mills MD, FACC, Senior Director,

Kathryn Gargiulo, RN, MPA, Associate Director

For the Janssen Cardiovascular Safety Group



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Introduction

- 2007 - J&J chartered the Cardiovascular Safety Group (CVSG).
 - Provide advice on potential or actual CV safety issues related to Johnson & Johnson pharmaceuticals and compounds of interest.
- Consultation is initiated by compound development team request; *not* required.
 - Representation: Clinical Pharmacology, Toxicology, Safety, Biometrics, Pharmacoepidemiology, Regulatory, Medical Affairs.
- We undertook this review to define the spectrum of CVSG activities over the past 6 years.

Background / Methods

- CVSG meets quarterly and *ad hoc* as needed.
- Detailed minutes: distributed to CVSG members and product team participants, and archived on a limited access website.
- We independently reviewed and collated all 2007-2012 meeting documents to classify the safety issues of concern.

Results:

29 Meetings, 35 Unique Compounds

Primary Concern (Potential Effect)	Number of Compounds
QT-Liability	18
Major Adverse Cardiac Events (MACE)*	5
Heart Rate/Blood Pressure Alterations	4
Regulatory Guidance Requested	4
Impairment of Ventricular Function	3
Drug-Drug Interaction	1
*MACE = stroke, myocardial infarction, death	

Conclusions

- QT-liability concerns accounted for 51% of the requests for CVSG consultation.
- A spectrum of concerns account for almost half of all consultations:
 - potential increases in MACE,
 - impairment of heart rate or blood pressure control,
 - interpretation of regulatory issues,
 - impairment of ventricular function.

Conclusions (Continued)

- Effective cardiac safety consultation
 - Is far more than discussion of QT-liability
 - Requires representation from multiple disciplines
 - Requires resources and support.

Discussion Questions

- How many cardiac safety committees are represented at this meeting?
- Have other committees compiled similar data?
- Is the spectrum of activity (half QT, half other) that we presented typical for these committees?
- Were the “other” broad issue categories similar?

Leadership and members

- How do we know what constitutes “best practice?”
 - Voluntary vs. mandatory reviews?
 - Should follow-up from teams be required?
 - Should chairs of these committees meet “off the record” to compare notes?
 - Does your committee have an annual budget?
 - Do you have administrative support for contact, schedule, and record-keeping?
 - How does the committee get feedback and improve?
 - How does the committee find qualified members?
- Action item: Would a CSRC-developed “Best Practices” document be useful?

Thank You!

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