

# Post Authorisation Safety Studies



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## **Format and content of the protocol, abstract and study report**

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*Information Day on Implementation of the New Pharmacovigilance Legislation*

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# Implementing Measure

**Content is based on a draft technical document  
which may be subject to revision**

Implementing Measure of Dir. 2001/83/EC Art. 108(g)  
and Reg. (EU) No 726/2004, Art. 87a(g)



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# Post Authorisation Safety Studies (PASS)

Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures.



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# Advice for Protocol Development

- Study should follow scientifically sound protocol
- Ethical principles
- Data Quality
- International Society for Pharmacoepidemiology:  
Guidelines for good Pharmacoepidemiology Practices  
[www.pharmacoepi.org](http://www.pharmacoepi.org)
- Transparency



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# Format of Study Protocol

- Title
- Marketing Authorisation Holder
- Responsible parties
- Amendments and updates
- Milestones



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# Title Page

**Protocol Title:** Chocolate intake and risk of cardiovascular disease: a **case control study** in **women aged 50-87**.

**Protocol Version:** V1.00

**Protocol Date:** 02/12/2011

**Principal Investigator:** Prof. John Crunchie, PhD, University of Bourneville, Birmingham, UK.

**Research Team:** Dr. Gerard Galaxy, PhD, Department of Epidemiology, Lindt University, Switzerland; Prof. Michael Hershey, University of Pennsylvania, USA.



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# Rationale and Background

- Description of safety hazard
- Description of safety profile or risk management measures that led to initiation of study
- Critical review of published and unpublished data



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# Research Question and Objectives

- Describe how the study will address the issue
- Pre-specified hypotheses
- Information to be gained from the study



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# Research Methods

- Study design (case control, cohort study)
- Setting
- Variables
- Data sources
- Study size
- Data management
- Data analysis
- Quality Control
- Limitations of research methods



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# Data Quality and Management



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# Protection of Human Subjects

- Provision for patient confidentiality and data protection
- Consideration for ethics committee review
- Procedures for informed consent if required



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# Reporting of Adverse Reactions

- Procedures for collection and management of adverse event/reaction reporting



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# Format of Study Protocol

- Communication of study results
- Resources required to conduct the study
- References
- Annexes



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# Format of Abstract

- Summary of study background, aims and design
- Should include research question, rationale for study, hypothesis, methods and main findings
- Follow same format as content of protocol



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# Format of Abstract

## Chocolate intake and the risk of cardiovascular disease: a case control study

**Background:** Randomised clinical trials have shown that chocolate intake reduces blood pressure and increases mood. The **aim** of this study was to investigate the association between chocolate intake and the risk of cardiovascular disease in women aged 50-87.

**Methods:** A **case control study** was conducted to investigate the association between chocolate consumption and cardiovascular disease. Dietary intake of chocolate and cardiovascular risk factors were assessed at baseline in **10, 011 women (aged 50-87)**. The women were already enrolled in a breast cancer screening programme. A case was defined as a woman who had a diagnosis of cardiovascular disease. Three controls were matched to each case based on age and index year of hospital admission. **Conditional logistic regression** was used to assess the relationship between chocolate consumption and cardiovascular disease. The study included a food frequency questionnaire, blood pressure measurements, baseline cardiovascular risk factors and prevalent diseases. Women who had pre-existing cardiovascular disease were excluded.

**Results:** There were 2210 women hospitalized for cardiovascular disease. Consumption of two bars of chocolate per day was associated with a **decreased risk of cardiovascular disease** (HR 0.32 95% confidence interval, 0.23-0.70).

**Conclusion:** Chocolate consumption was associated with decreased risk of cardiovascular disease in women aged 50-87 who consumed chocolate at least once per day.



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# Format of Final Study Report

- Same format as study protocol
- Focus on methods, results and data quality
- Include limitations and efforts to address potential sources of bias



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# Format of Final Study Report

- Describe all statistical methods applied, how missing data were addressed, any sensitivity analysis
- Describe any amendments of analysis plan included in study protocol
- Describe mechanisms to ensure data quality and integrity



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# Results

- Participants
- Descriptive data
- Outcome data
- Main results
- Other analysis
- Adverse events/reactions



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# Discussion

- Key results
  - Limitations
  - Interpretation
  - External validity
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- References
  - Other information



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# Thank You



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