

# CLINT

Facilitating International Clinical Trials in Stem  
Cell Transplantation

**Implementation of the Clinical Trials Directive:**

**Regulatory and Ethical Issues  
Workshop**

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Florence, 2 April 2008

# Questionnaire

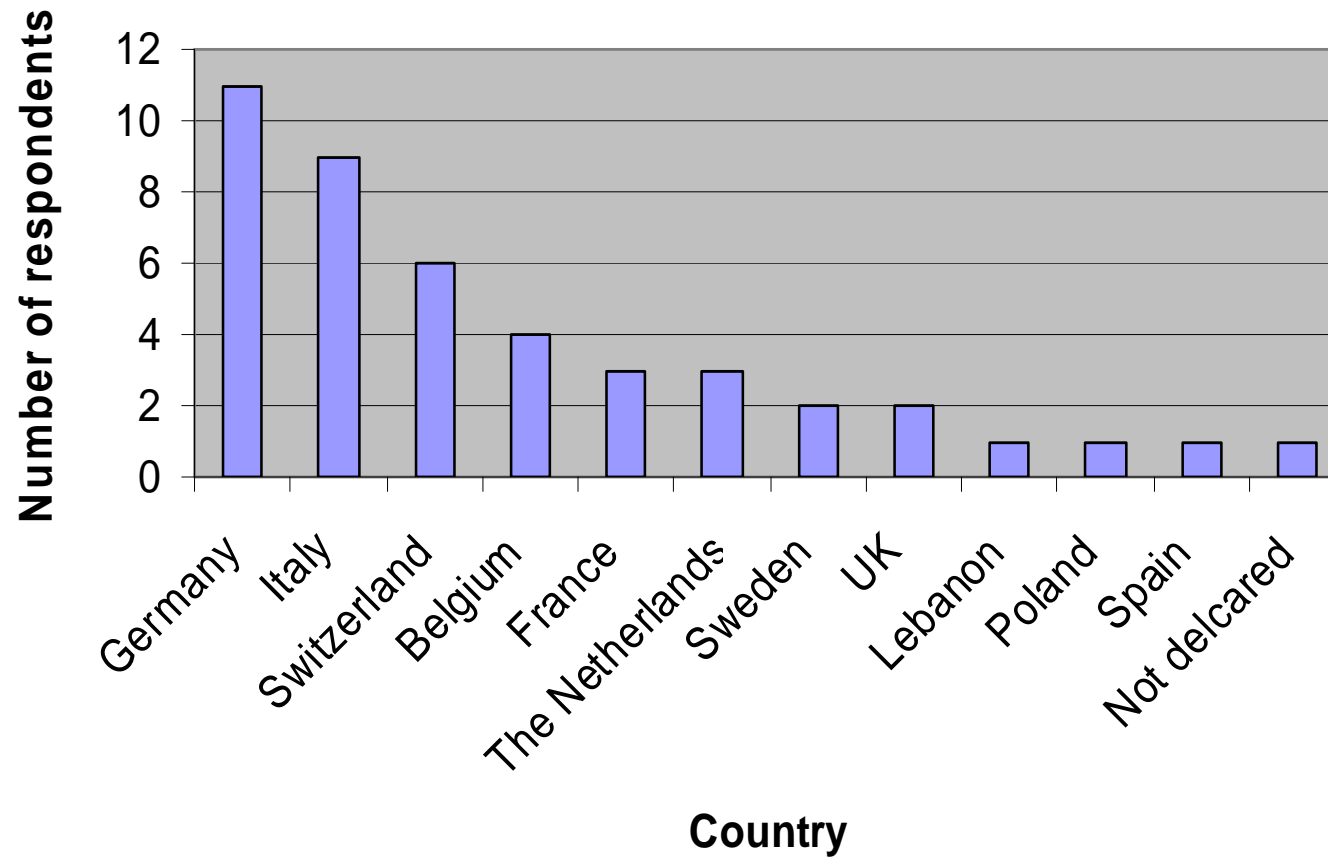
- Personal experience and background
- Perceived impact of the Directive on numbers of clinical trials at institutional and national level.
- Impacts of the directive on:
  - Safety
  - Definitions
  - Sponsorship
  - Harmonisation
  - Time to EC/CA and first patient
  - Trial costs
- Recommendations for improving procedures for prospective clinical trial.

# Responses

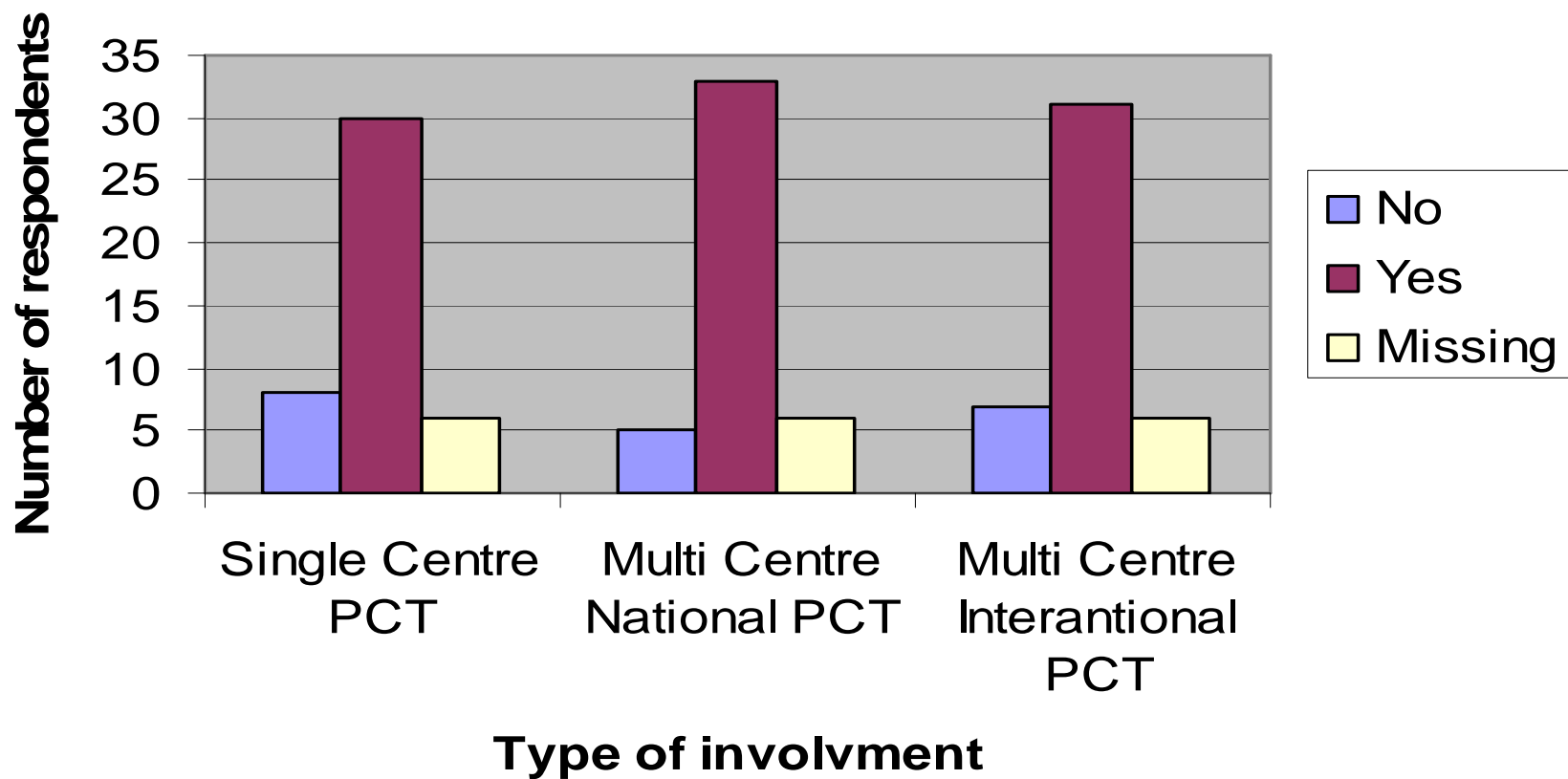
- All EBMT members in EU countries plus Switzerland and Norway invited to participate.
- 44 responses received
- 11 countries (1, Lebanon, out of scope).



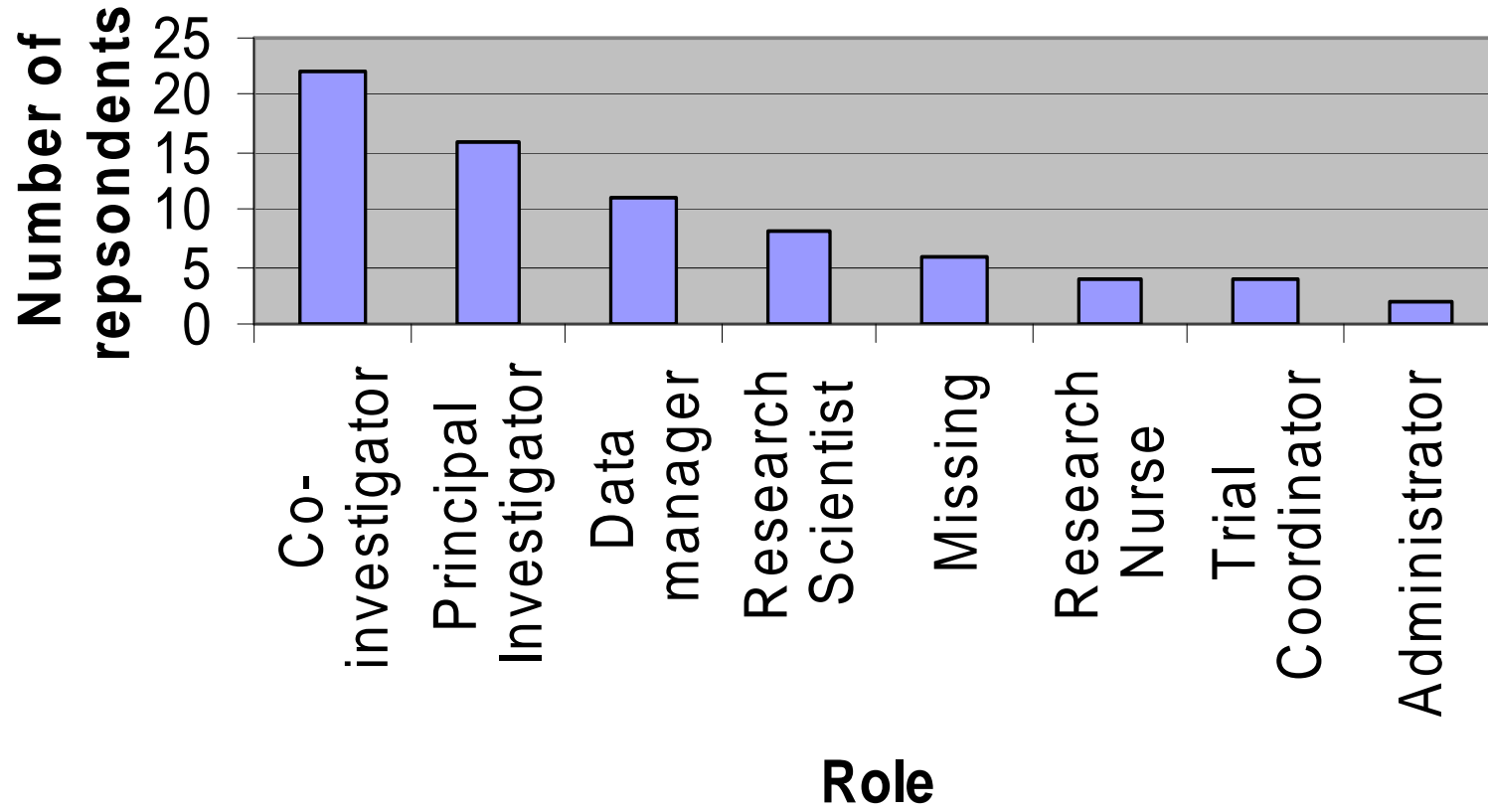
## Number of respondents by country



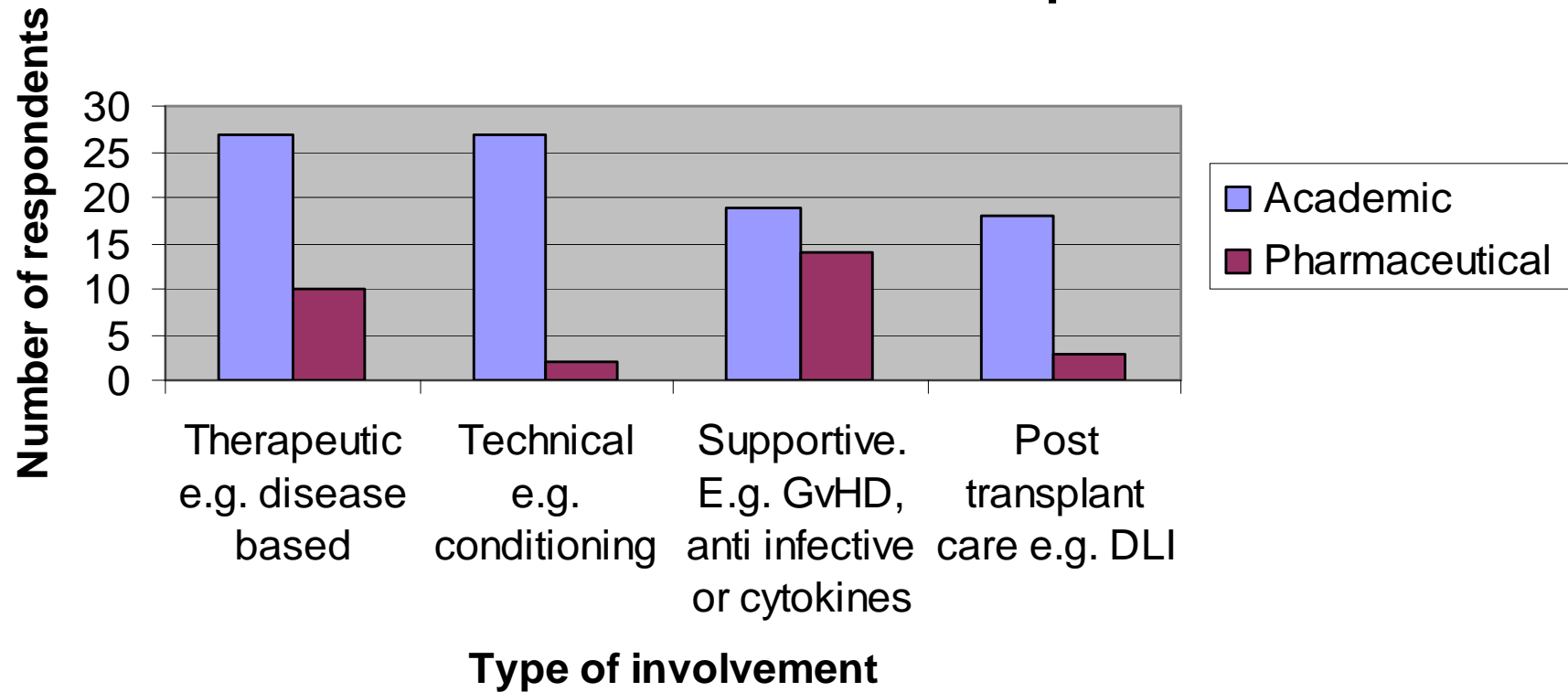
## Personal involvement in prospective clinical trials related to stem cell therapy



# Type of involvement in prospective clinical trials related to Stem Cell Transplantation



## Respondent experience of prospective clinical trials related to Stem Cell Transplantation

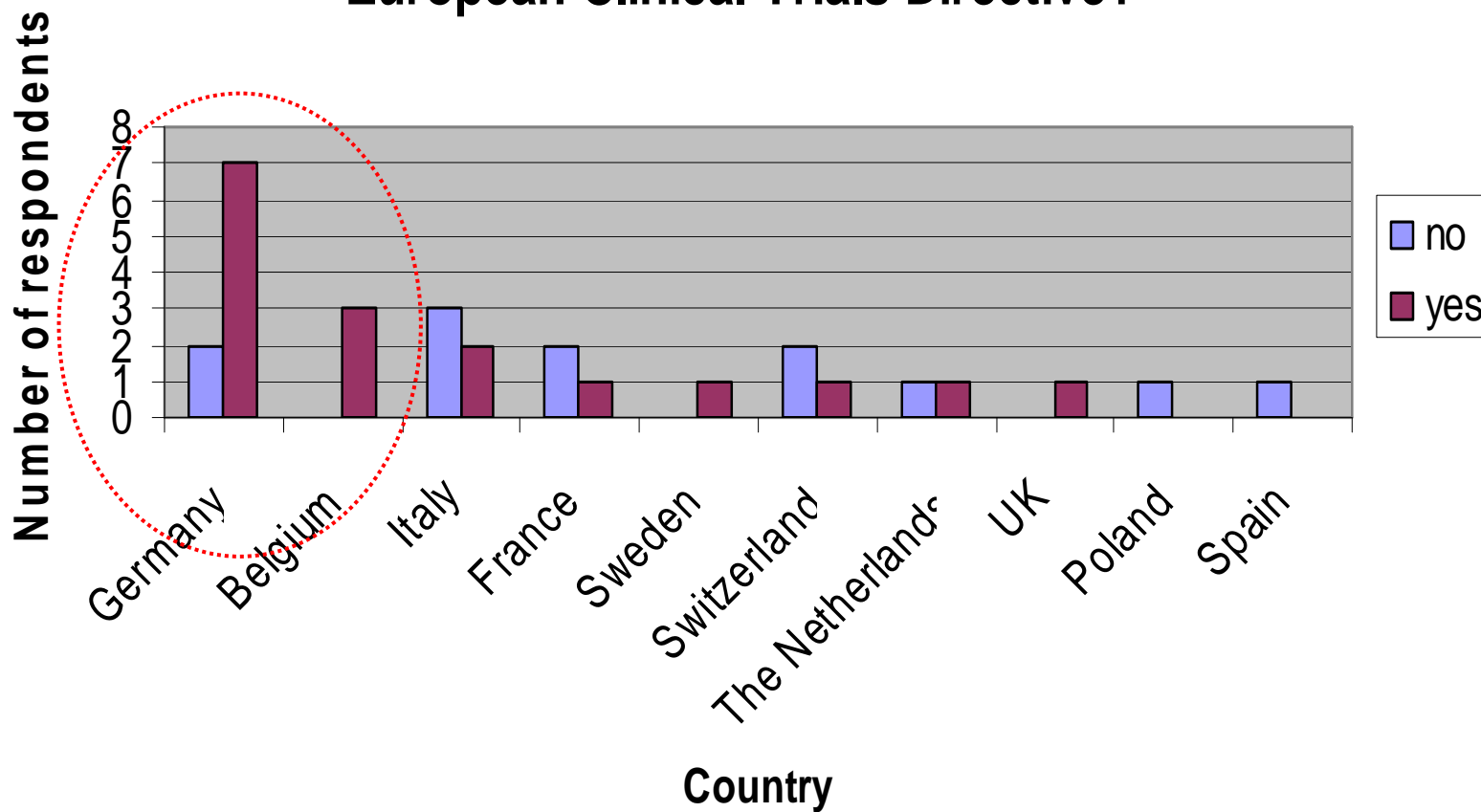


**Seven participants reported involvement in both academic and pharmaceutical clinical trials, but did not state which type.**

# Impact at Institutional Level

- Germany and Belgium
  - majority of respondents reported a decrease in SC Transplantation clinical trials following implementation of the Directive.
- Italy, France and Switzerland
  - not appear to be the case.

## Reduced institutional involvement following the European Clinical Trials Directive?

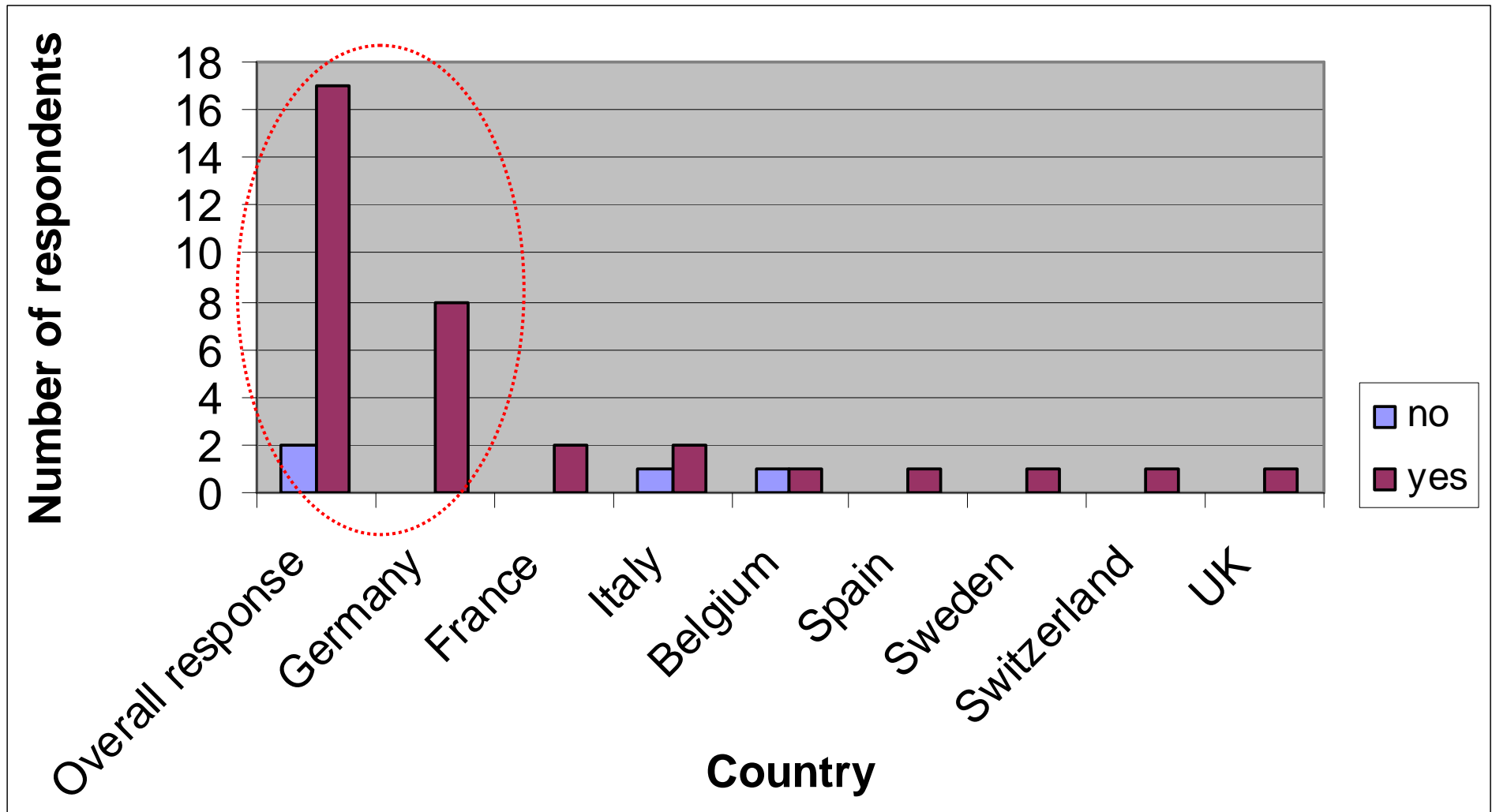


Respondent's own institute

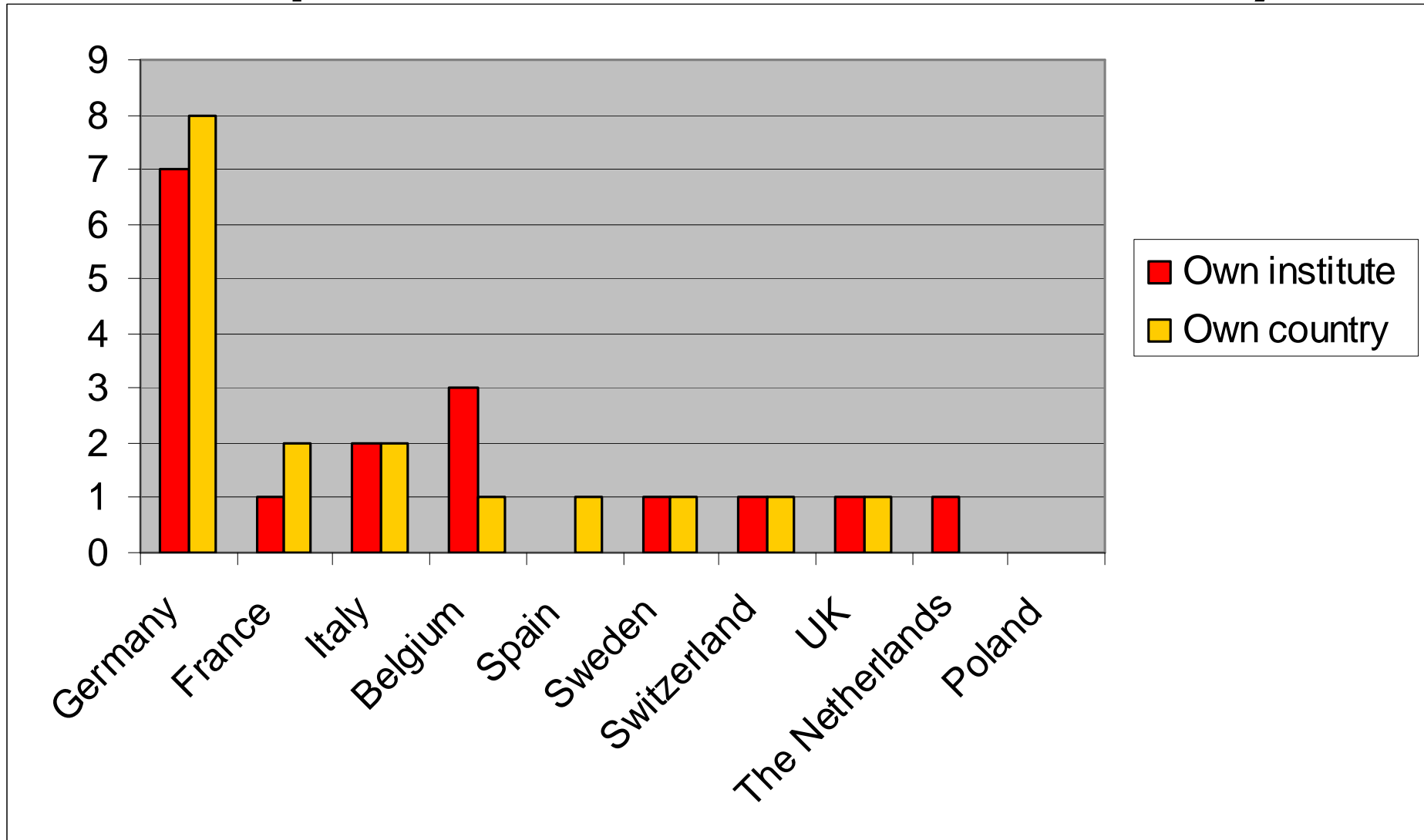
# Impact at National Level

The overwhelming majority of respondents believe that at a national level the numbers of clinical trials have decreased since implementation of the Directive.

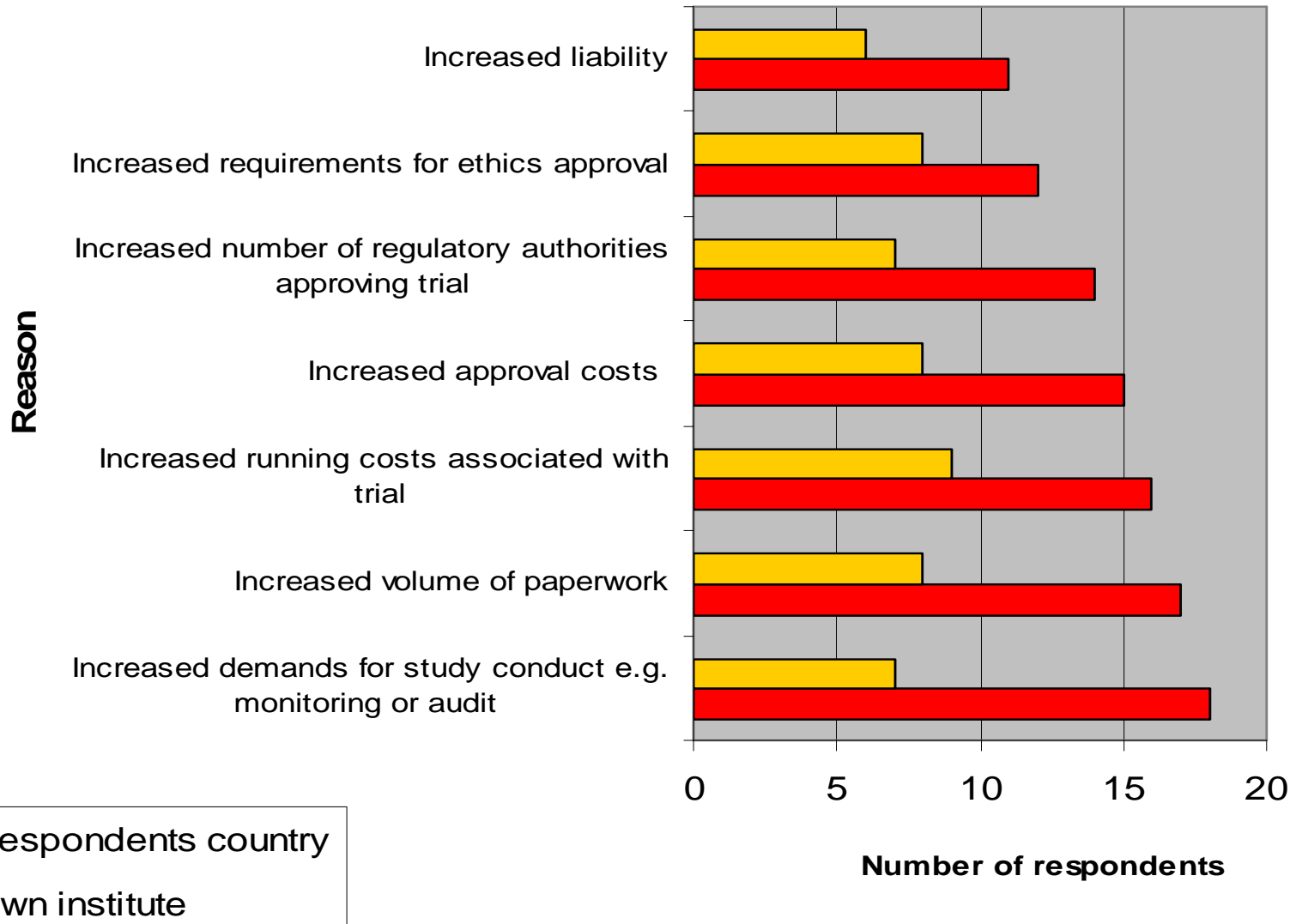
# Reduction in Number of Prospective Clinical Trials at a National Level?



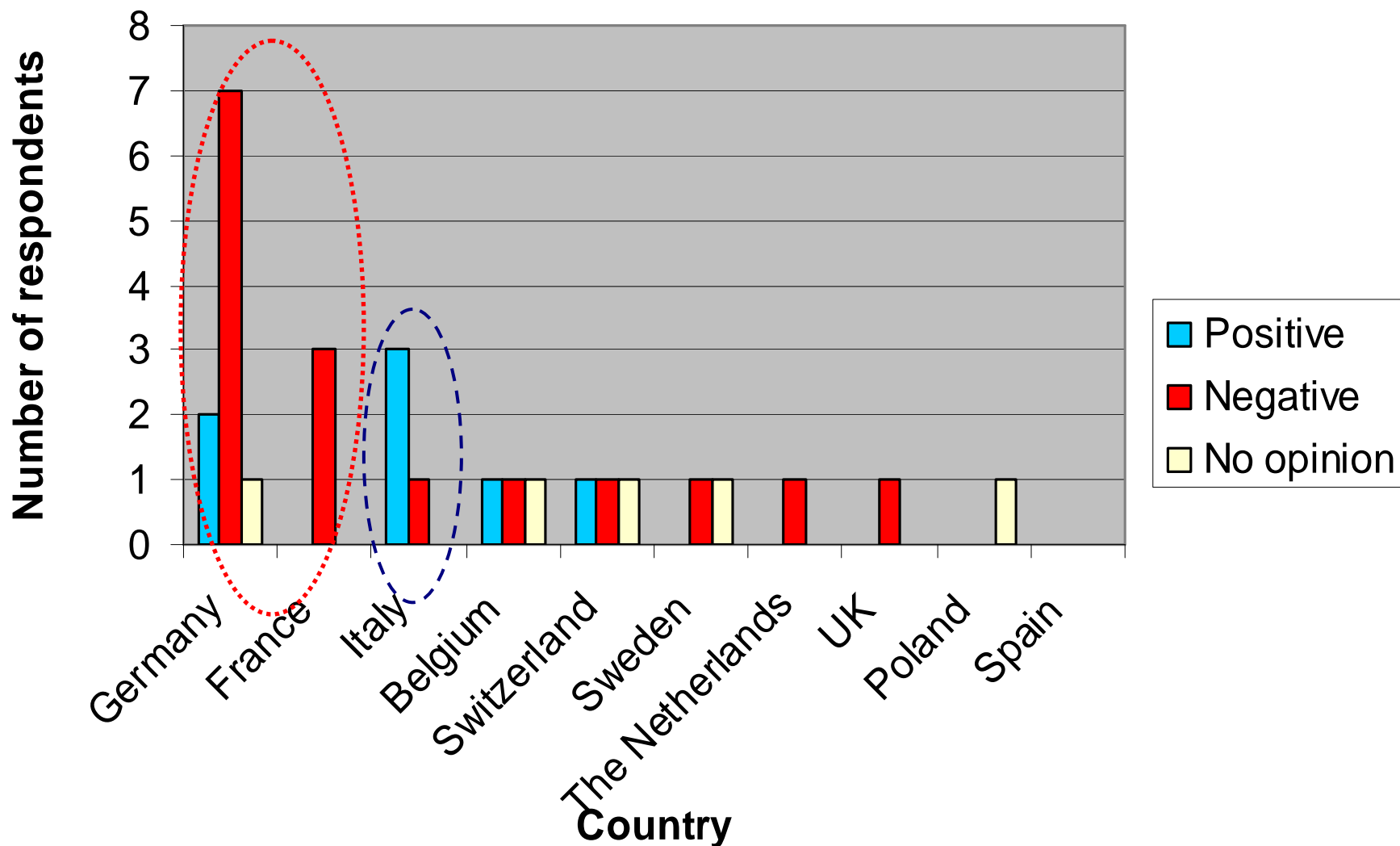
# No of respondents reporting a reduction in number of prospective clinical trials in both respondents own institute and country



## Reasons for reduced institutional involvement following implementation of European Clinical Trials Directive



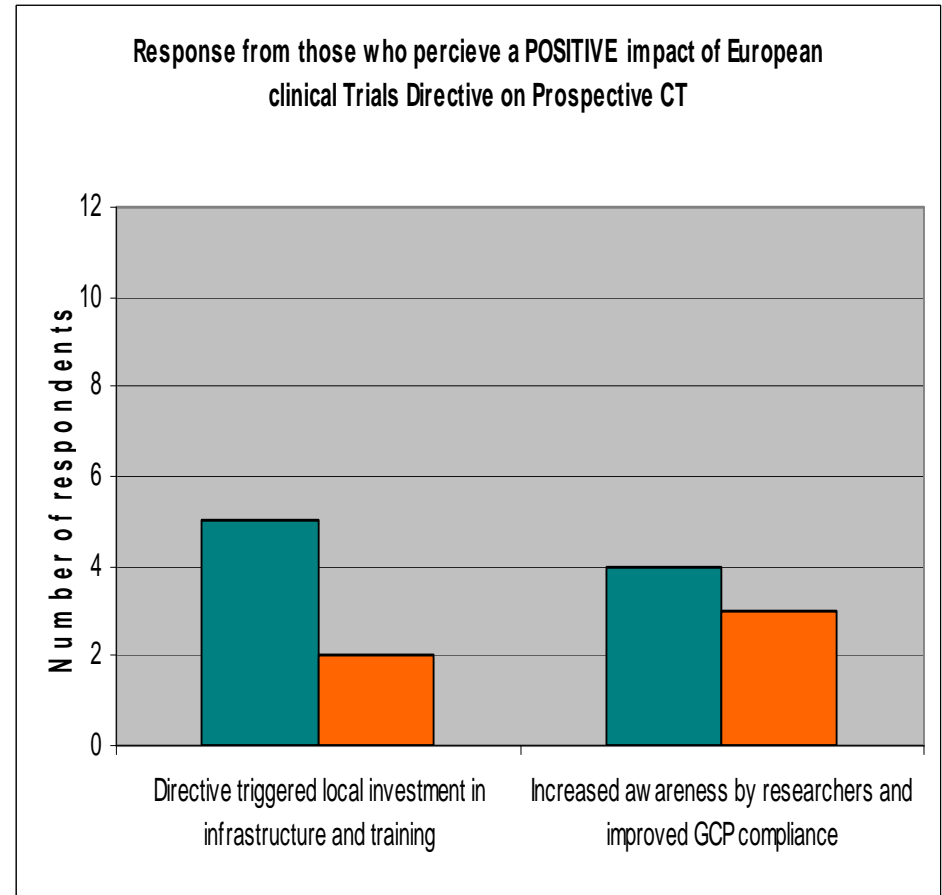
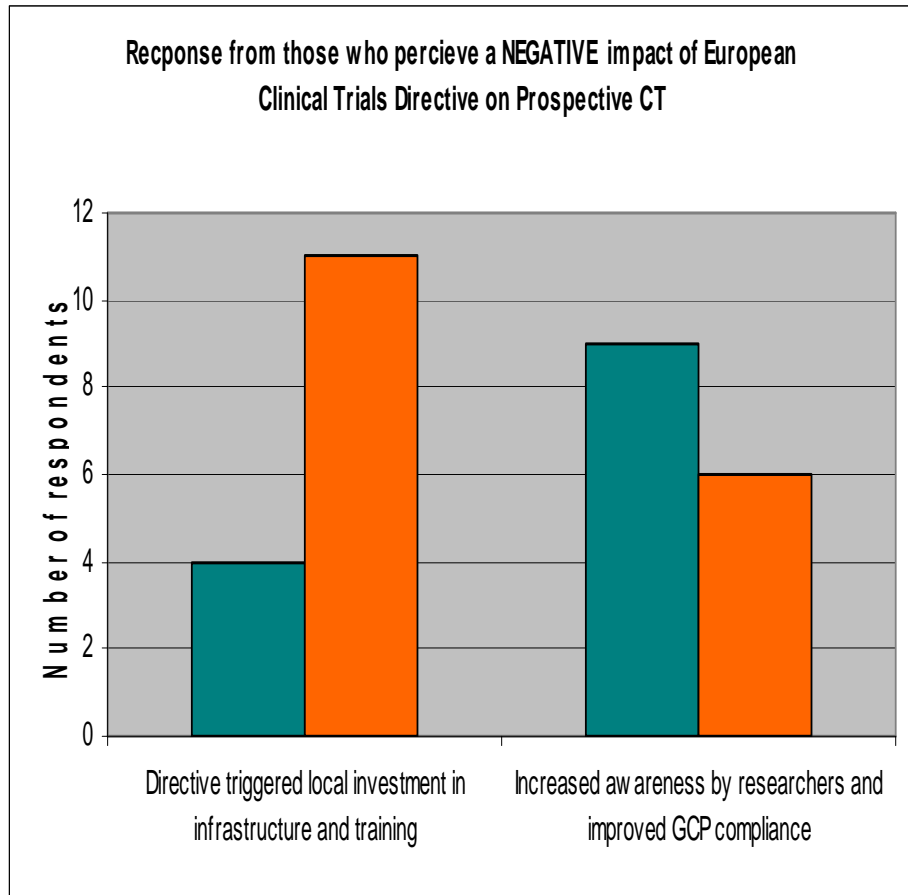
# What effect has the European Clinical Trials Directive had on prospective Clinical trials related to stem cell transplantation?





# Impact on Training and Researcher Awareness

- Majority do *not* perceive implementation of the Directive as having triggered local investment in training.
- Most respondents perceive that the implementation of the Directive has increased researcher awareness and greater GCP compliance.

# Impact of European Clinical Trials directive on Training

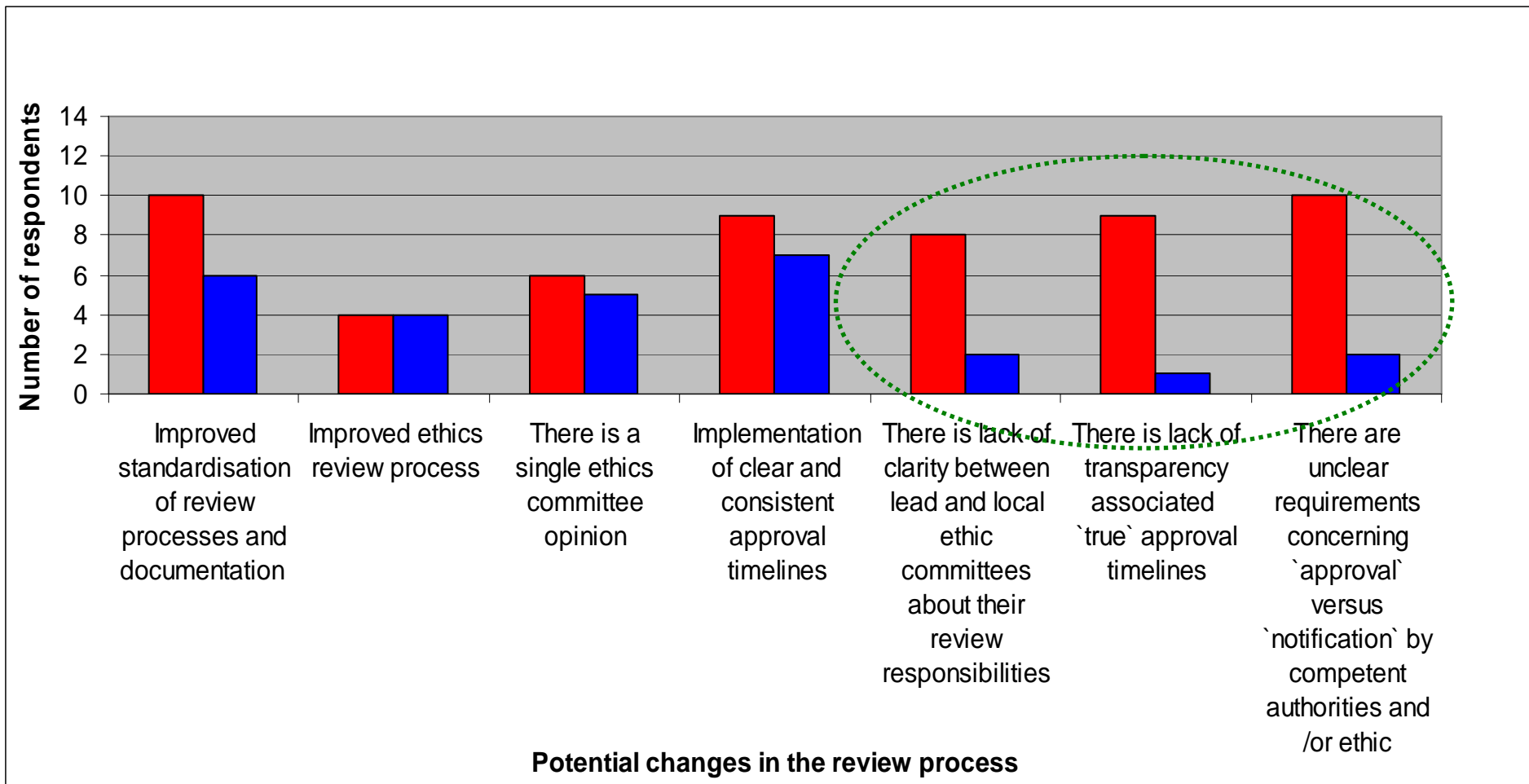


 Agree  
 Disagree

# The Review Process

Respondents were asked whether they agreed or disagreed with a number of statements on the review and approval process.

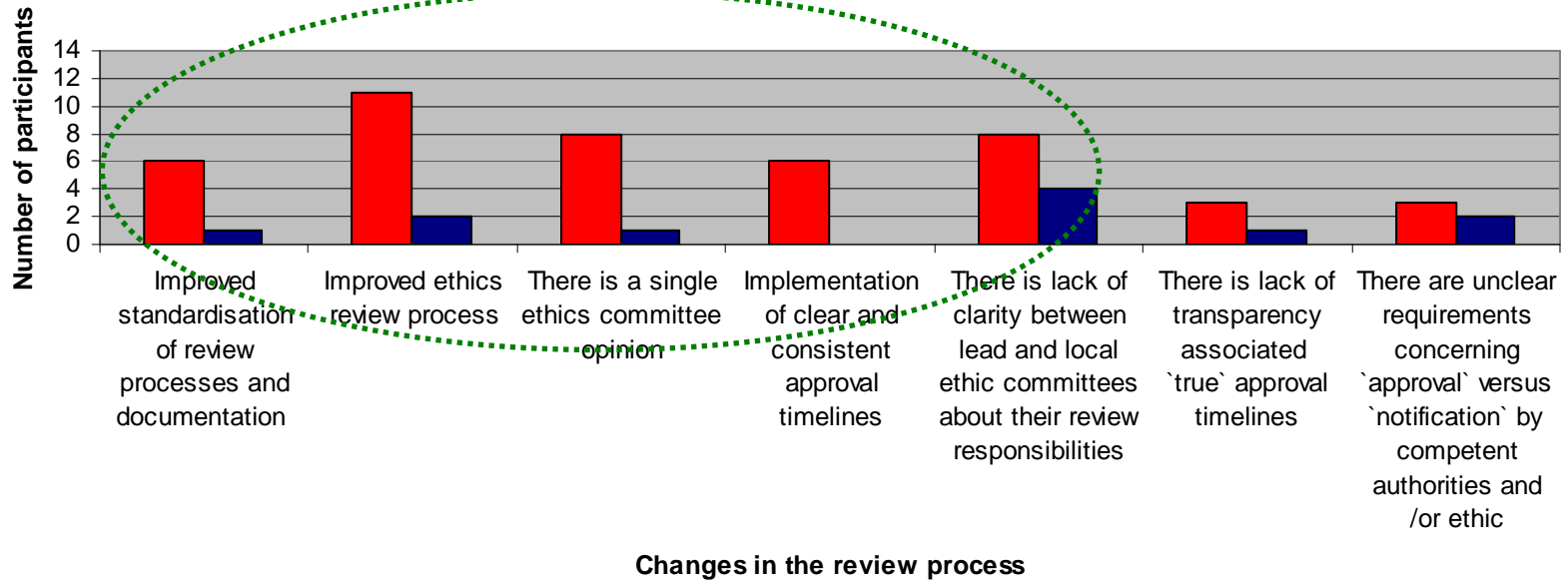
# Agreement with statements associated with the review processes following implementation of the European Clinical Trials Directive



■ Perceived NEGATIVE impact on PCT

■ Perceived POSITIVE impact on PCT

### DISAGREEMENT with statements associated with the review process following the European Clinical Trials Directive



Perceived NEGATIVE impact on PCT  
 Perceived POSITIVE impact on PCT

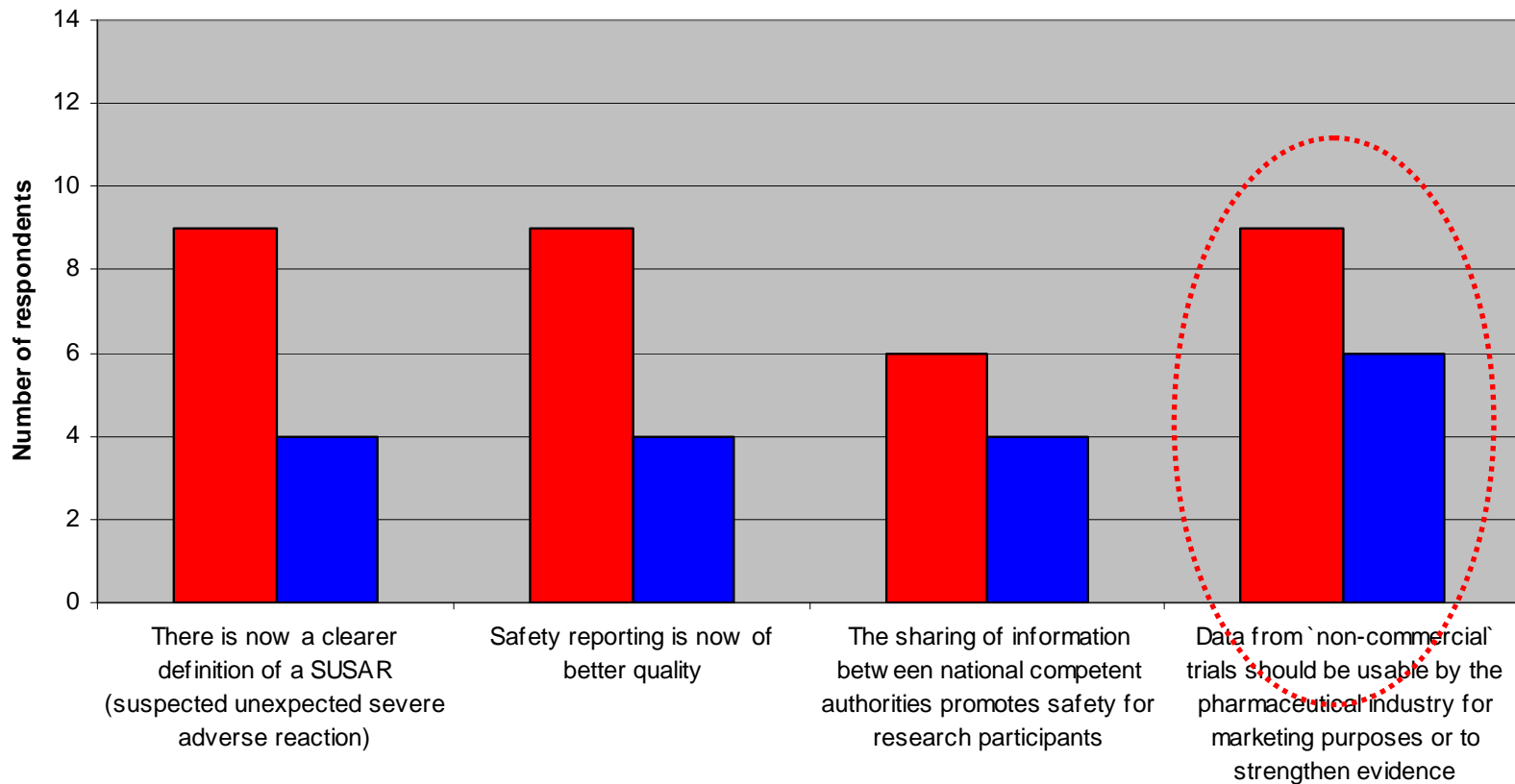
# Impact on Safety

Majority believe that:

- There is now a clearer definition of a SUSAR
- Safety reporting has improved
- Data from “non-commercial trials should be useable by Pharma

The majority do not believe that sharing of information by CAs improves patient safety.

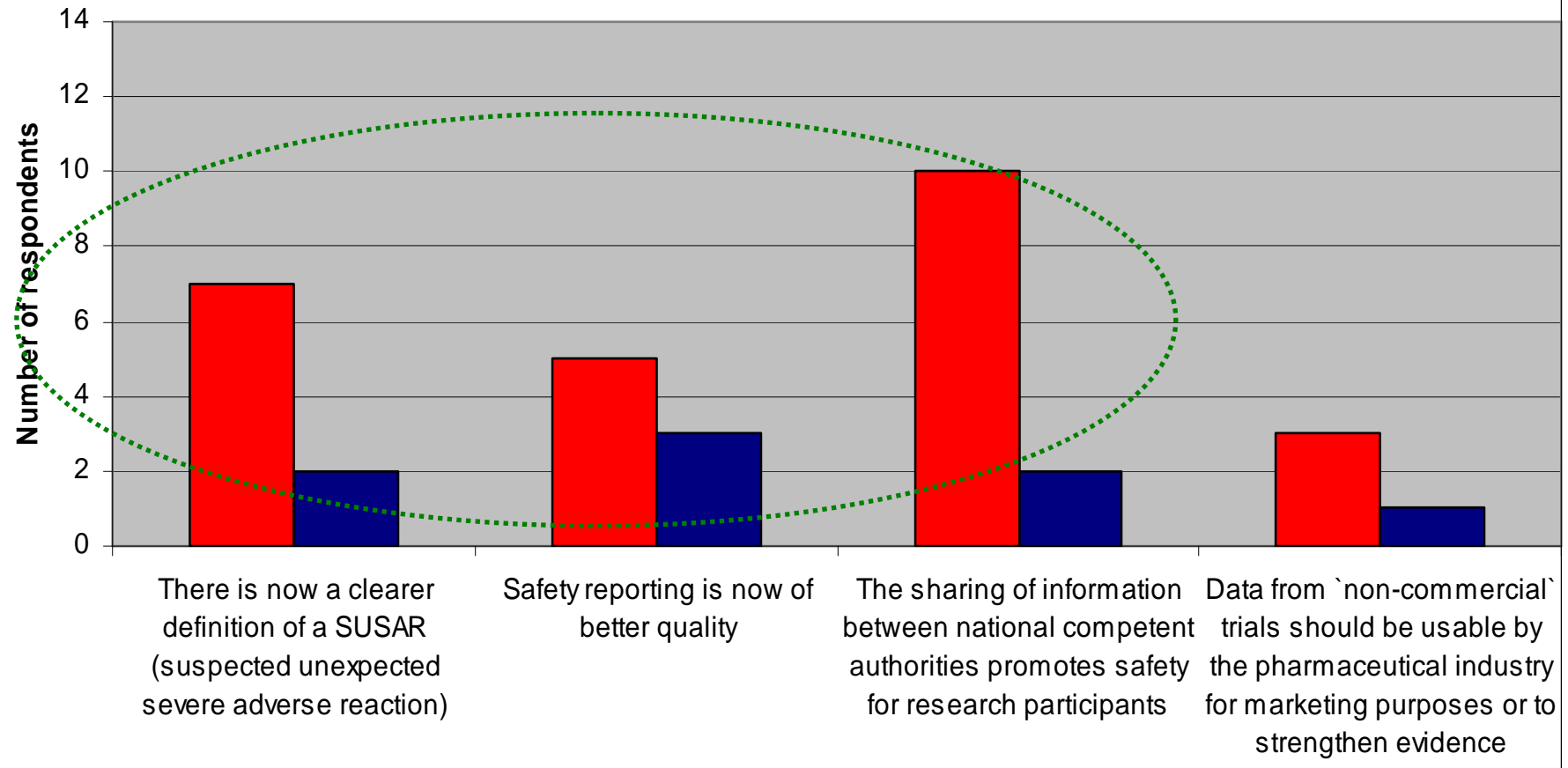
### AGREEMENT with the statements associated with SAFETY following the European Clinical Trials Directive





 Perceived NEGATIVE impact on PCT

 Perceived POSITIVE impact on PCT

## DISAGREEMENT with the statements associated with SAFETY following implementation of the European Clinical Trials Directive



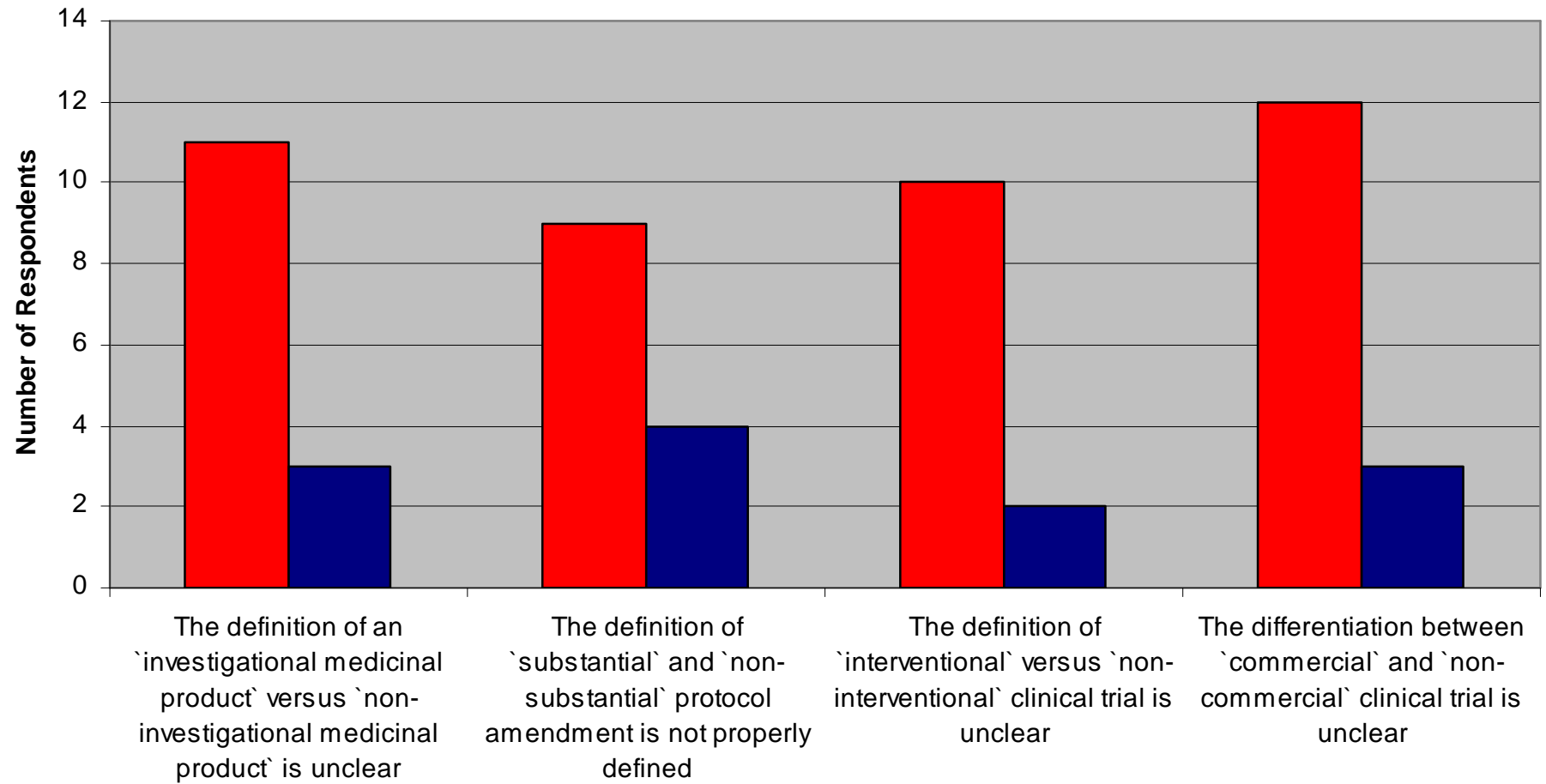
 Perceived NEGATIVE impact on PCT

 Perceived POSITIVE impact on PCT

## **Impact on Definitions**

Majority of respondents believe that implementation of the Directive has not led to any clarification of definitions and that these remain unclear.

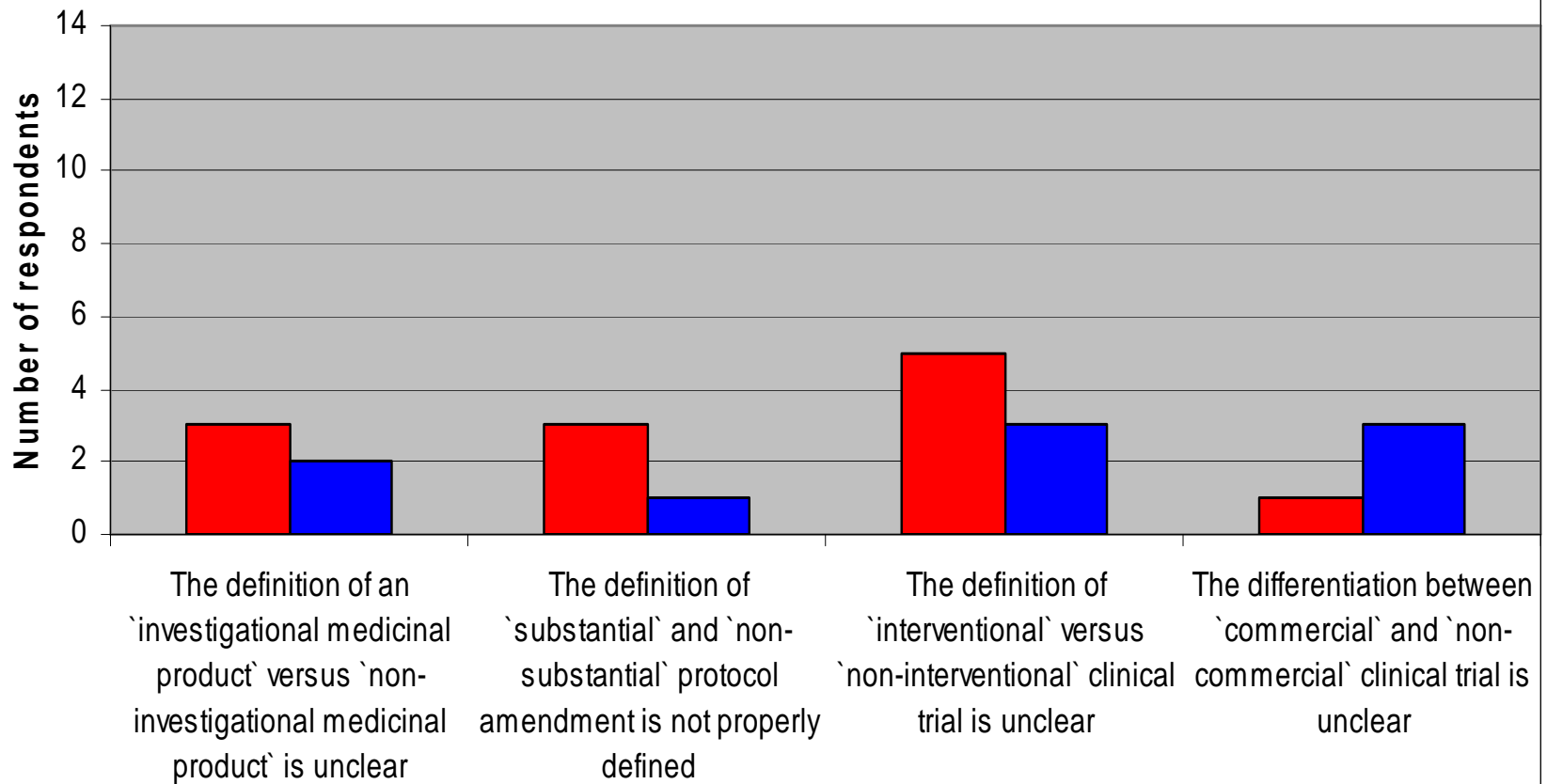
### Agreement with statements associated with DEFINITIONS following implementation of the European Clinical Trials Directive



 Perceived NEGATIVE impact on PCT

 Perceived POSITIVE impact on PCT

### DISAGREEMENT with statements associated with DEFINITIONS following the implementation of the European Clinical Trials Directive



 Perceived NEGATIVE impact on PCT

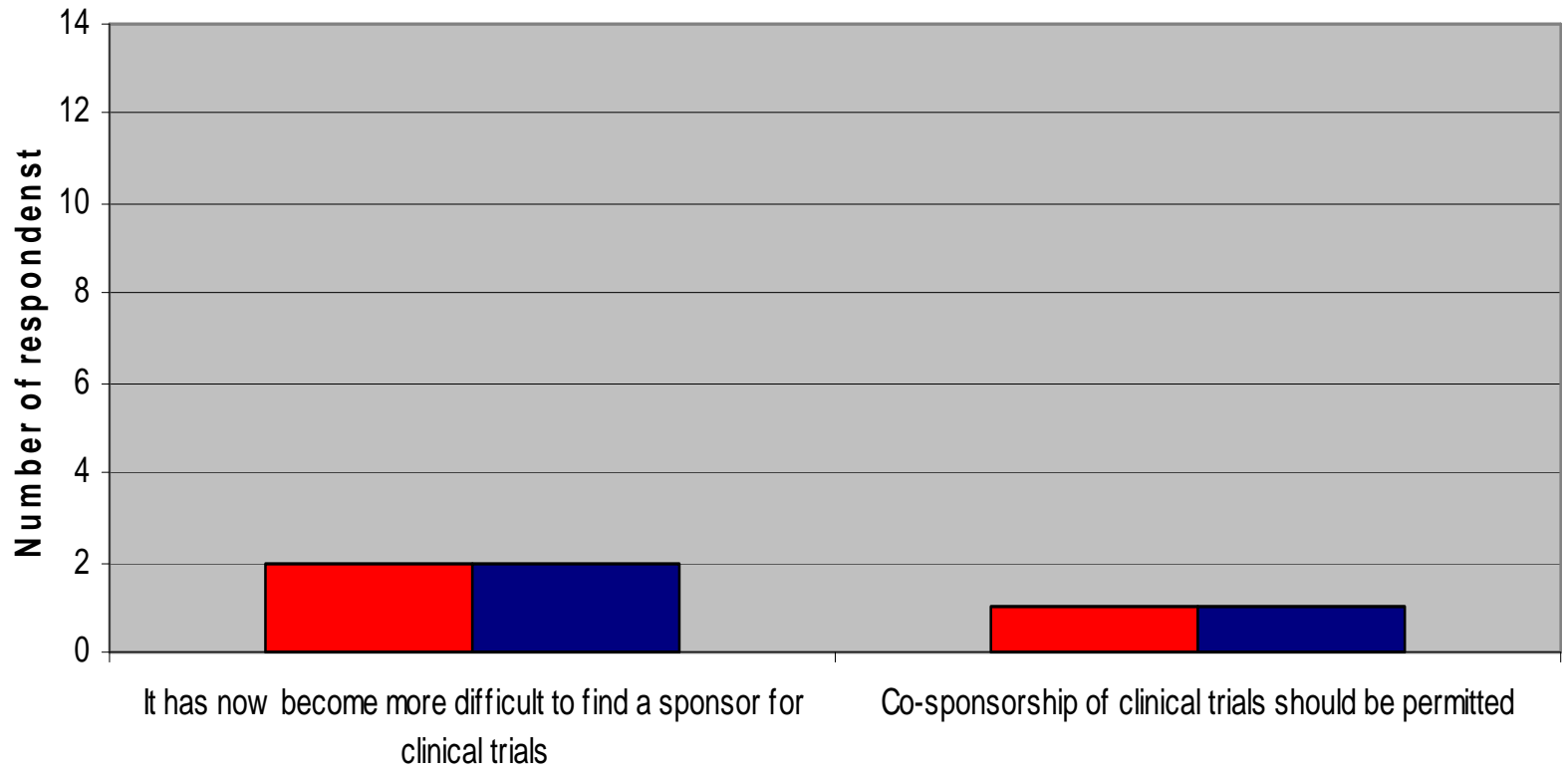
 Perceived POSITIVE impact on PCT

# Impact on Sponsorship

The majority of respondents agree that:

- It is now much more difficult to find a sponsor for a clinical trial
- Co-sponsorship should be permitted

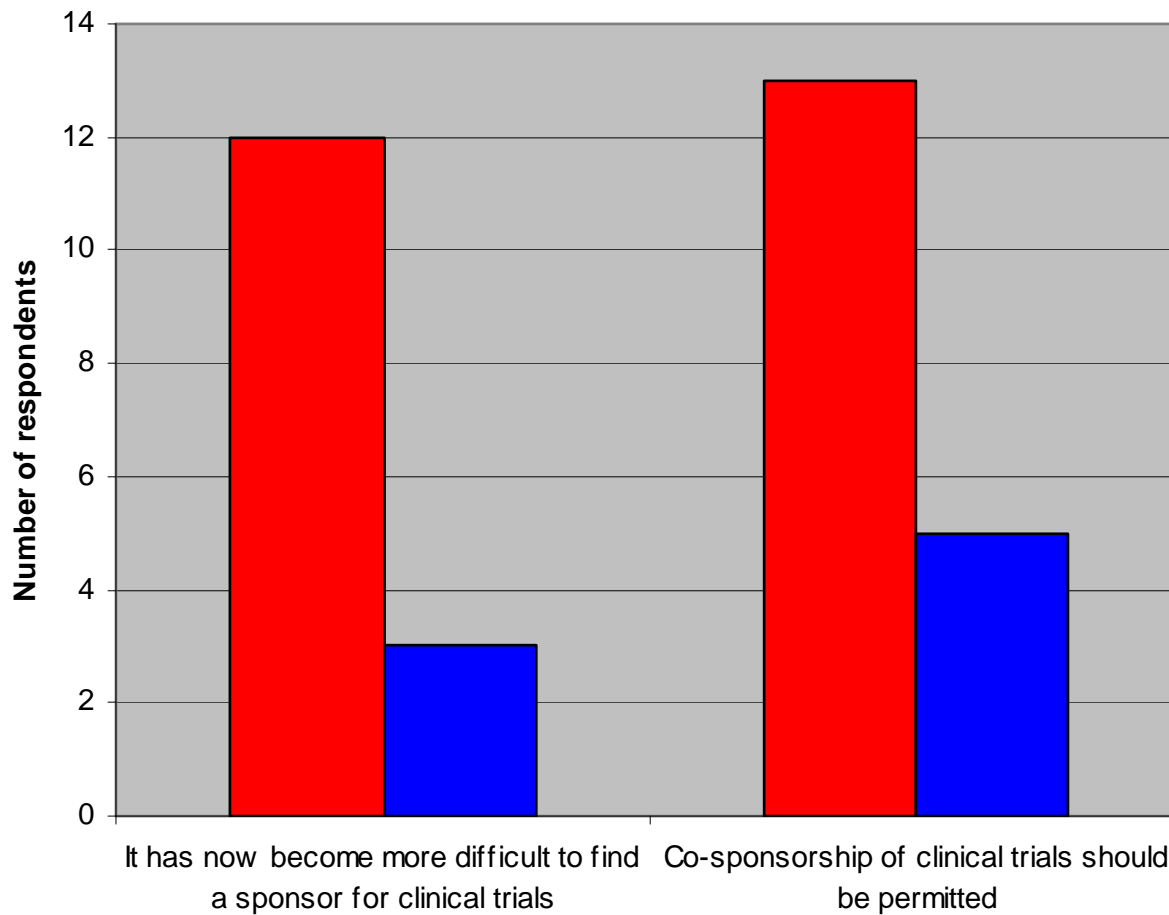
### DISAGREEMENT with statements relating to SPONSORSHIP following the European Clinical Trials Directive



 Perceived NEGATIVE impact on PCT

 Perceived POSITIVE impact on PCT

**AGREEMENT with statements relating to SPONSORSHIP following the European Clinical Trials Directive**



 Perceived NEGATIVE impact on PCT

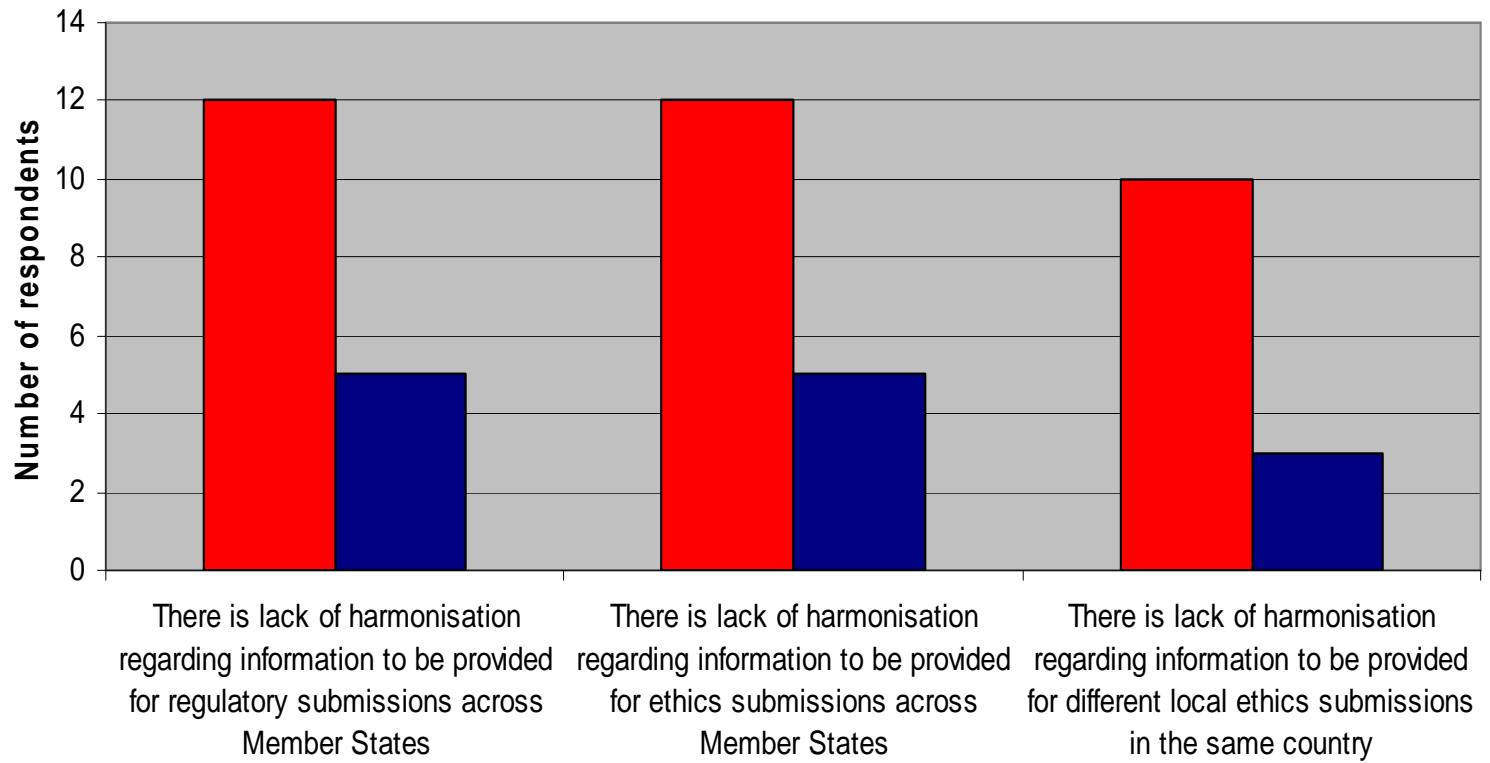
 Perceived POSITIVE impact on PCT



# Impact on Harmonisation

The majority of respondents feel that the implementation of the Directive has *not* addressed lack of harmonisation in respect of information that needs to be provided for approvals either:

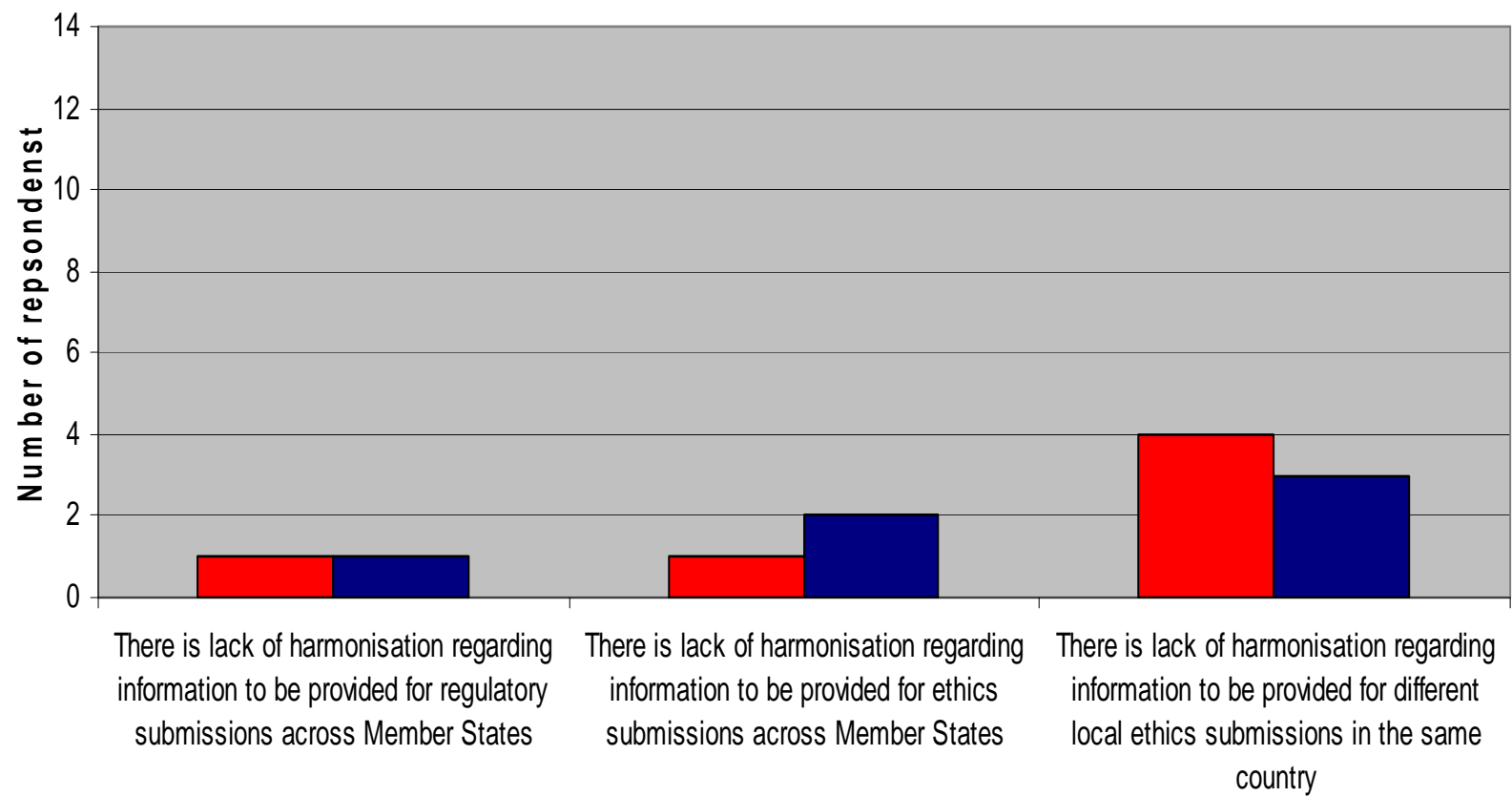
- between Member States or
- between local ethics committees within individual countries

### AGREEMENT with statements relating to EUROPEAN HARMONISATION following the implementation of the European Clinical Trials Directive



 Perceived NEGATIVE impact on PCT  
 Perceived POSITIVE impact on PCT

### DISAGREEMENT with statements relating to European Harmonisation following the implementation of the European Clinical Trials Directive



 Perceived NEGATIVE impact on PCT

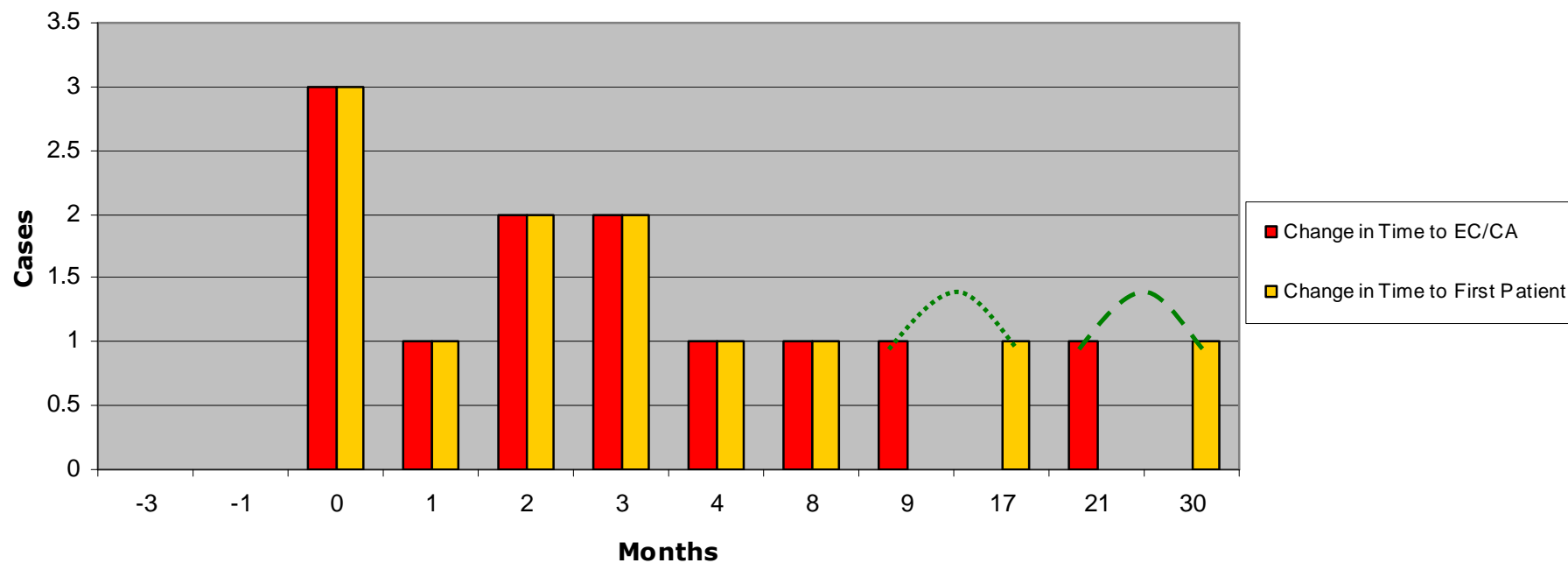
 Perceived POSITIVE impact on PCT

# Time to Implementation

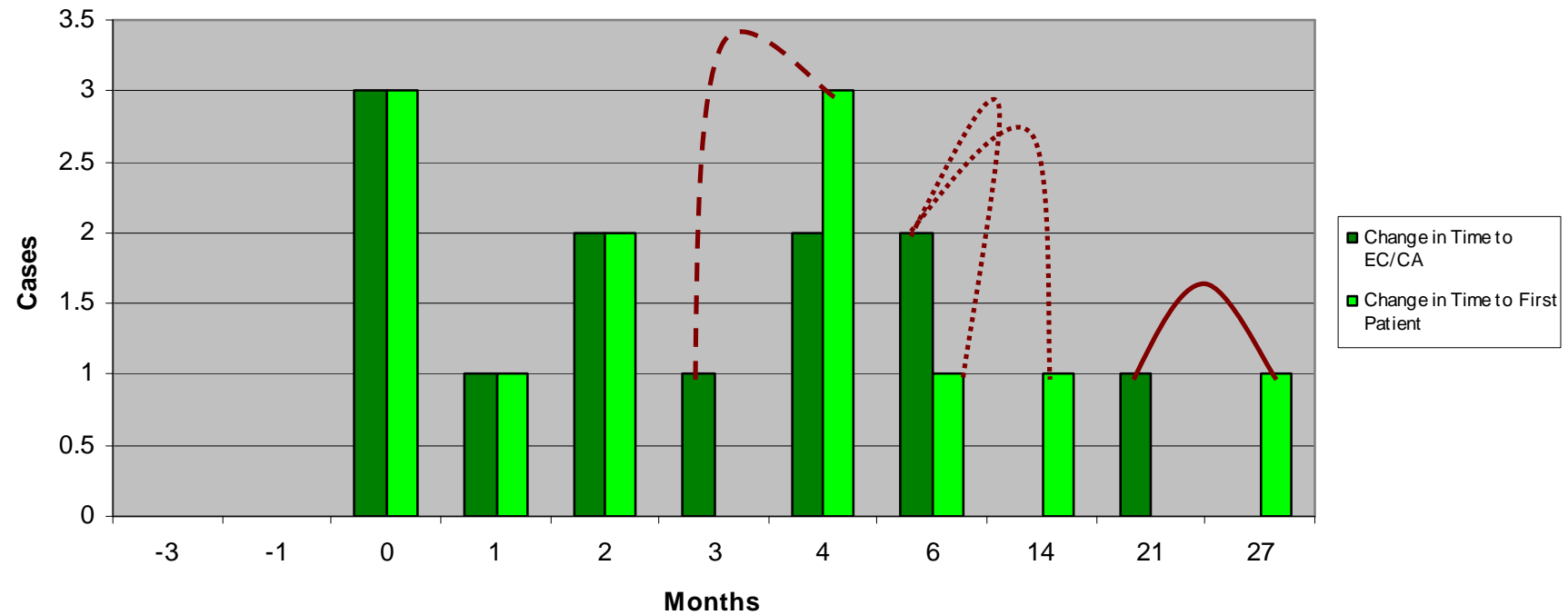
Following implementation of the Directive, it takes longer to obtain EC/CA in all countries and for all categories of Clinical Trial

# Changes in time taken to EC/CA and first patient since implementation of the Directive for

## Single Centre Studies

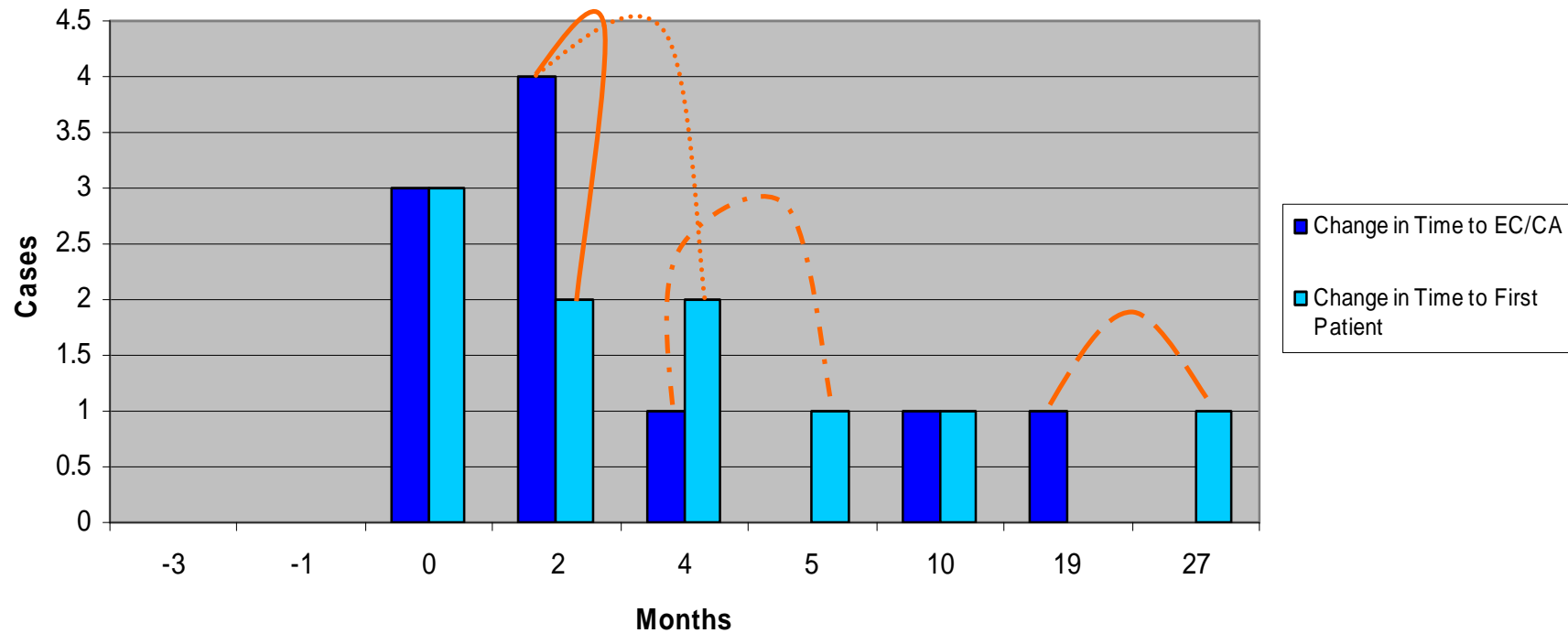


# Changes in time taken to EC/CA and first patient since implementation of the Directive for National Multicentre Studies



# Changes in time taken to EC/CA and first patient since implementation of the Directive for

## International Multicentre Studies



# Recommendations regarding better facilitation of prospective clinical trials (1).....

- **Insurance**
  - Insurance fees are too high
  - Length of required institutional insurance is too long (up to ten years e.g. Italy)
- **Bureaucratic process**
  - Too much paper work
  - Less administration
  - More focus on the scientific or clinical background of a study, less on legal implications
- **Funding**
  - Easier to obtain
  - Install proper funding for trials
  - More readily available support from the EU for translational type clinical research funding
  - Provide sufficient public funding
  - Provide ethical and regulatory approval free of charge for academic institutions

Recommendations regarding better facilitation of prospective clinical trials (2).....

## **Approval process**

- Work on sponsoring and centralisation of documents needed for approval
- Reduce the degree of monitoring required for investigator led trials.
- Harmonize legislation for EU-members
- One central ethics and regulatory body for all member states
- Reduce the number of Ethics committees e.g. cantonal committees in Switzerland

# Summary of Preliminary Observations and Conclusions

- Since implementation of the Directive, it takes longer to obtain EC/CA in all countries and for all categories of Clinical Trial.
- The perceived negative impact of the CT Directive is greatest in Germany.
- Italy appears relatively satisfied with the implementation of the CT Directive.
- There is perceived to be a *reduction* in the number of prospective clinical trials at a national level since implementation
  - (not always reflected in the respondents response about their own institute).

# Summary of Preliminary Observations and Conclusions (2)

The main reasons for reduction in CT activity appear to be:

- Increased administrative burden
- Increased running costs and liability costs are also a concern
- Increased requirements for EC/CA approval

# Summary of Preliminary Observations and Conclusions (3)

- Most respondents are not convinced that implementation of the Directive has triggered local investment in infrastructure and training.
- Most do however believe that researchers are more aware and GCP compliance has improved.

# Summary of Preliminary Observations and Conclusions (4)

## Implementation of the Directive:

- Positive impact on safety
- Not resulted in
  - improvements in definitions
  - improved harmonisation of regulatory requirements.
- Negative impact on researcher ability to find sponsors.
  - Co-sponsorship should be permitted.

# Caveats

- Questionnaire was too long
- Further data analysis in progress
- The sample size is too small to make nationally-based judgements.

# Lessons and Plans

- Treat this exercise as a pilot.
- Circulate a second MUCH SHORTER questionnaire in about 2 months time to gather more data to address key issues identified from analysis.
- Contact *named individuals* to improve response rate.

# Aims of BREAKOUT GROUPS

- To contribute to the analysis
- To gather more data
- To identify policy options