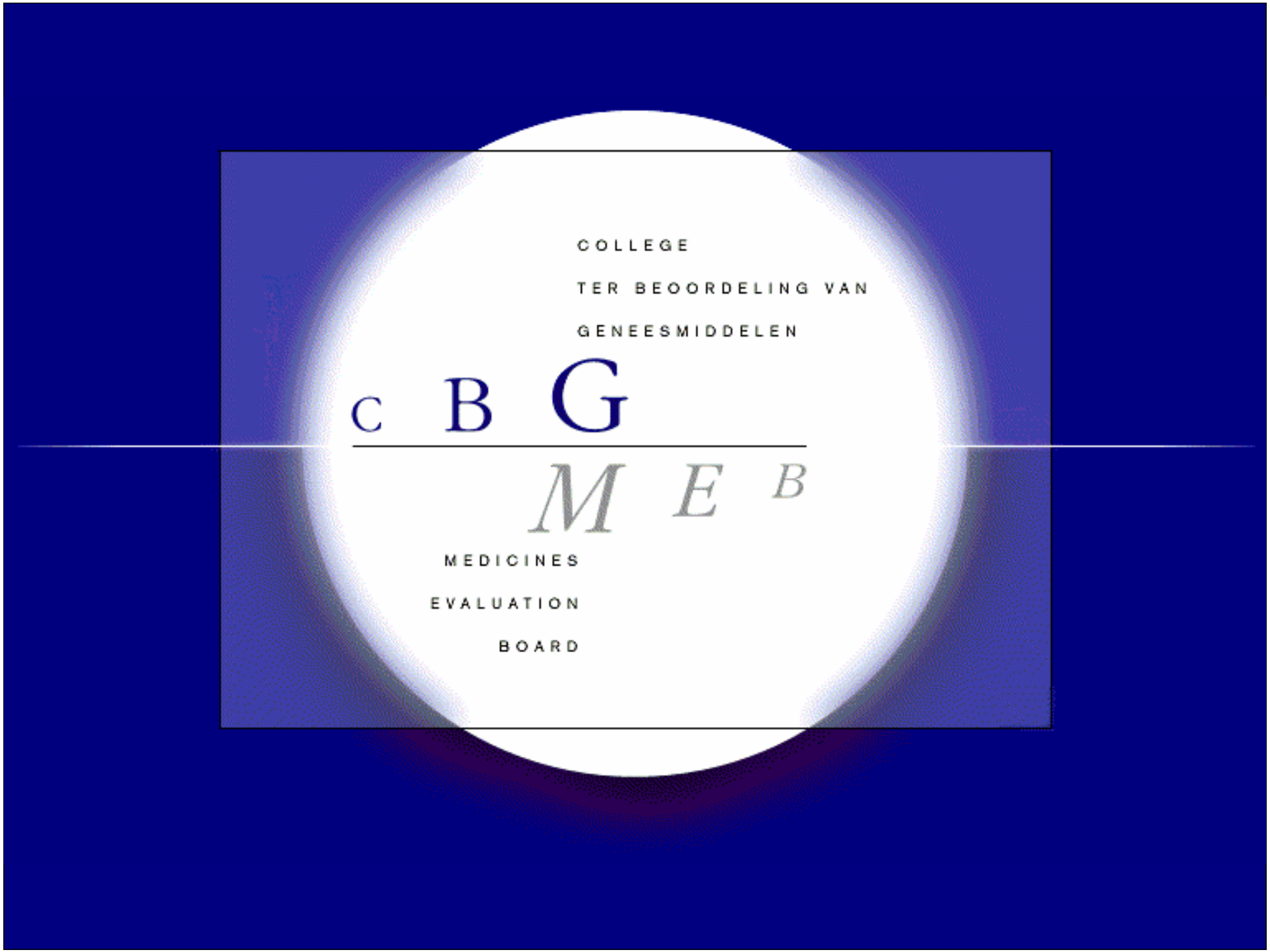
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EU Variations Regulation

Consequences for competent authorities-
Will the change simplify administrative hurdles?

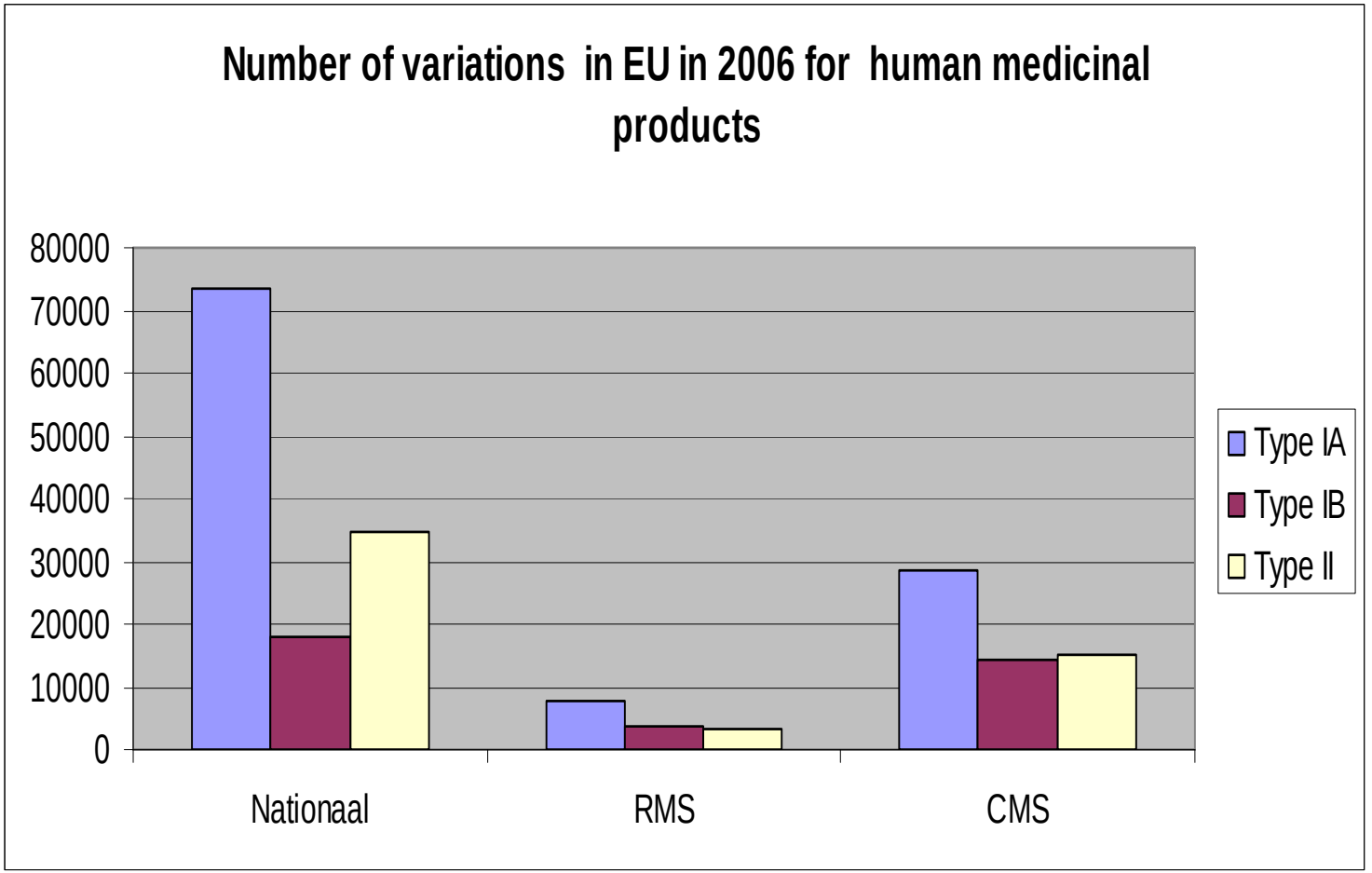
Truus Janse-de Hoog
Medicines Evaluation Board
Chair CMD(h)

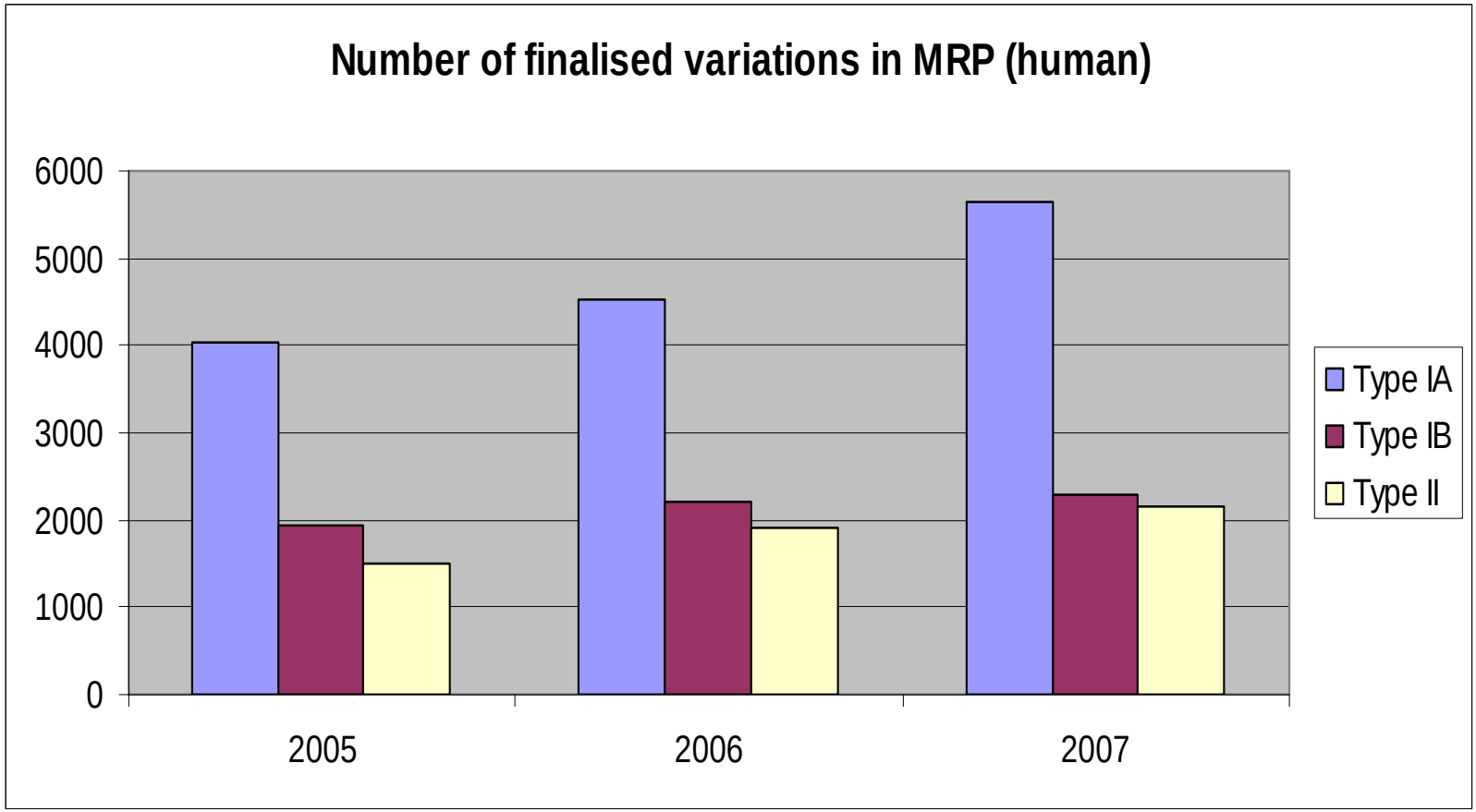
EU Variations Regulations

The European perspective

- Current situation
- Proposed changes and role of CMD(h)
  - Worksharing
  - Arbitration
  - Scientific recommendations for unforseen variations

- *Simplification or administrative burden?*


Number of variations in EU in 2006 for human medicinal products
80000
70000
60000
50000
40000
30000
20000
10000
0
Nationaal
RMS
CMS
Type IA
Type IB
Type II


Number of finalised variations in MRP (human)
6000
5000
4000
3000
2000
1000
0
2005
2006
2007
Type IA
Type IB
Type II

Worksharing

Proposal Variation Regulation

In order to avoid duplication of work in the evaluation of variations a Worksharing procedure should be established under which one authority, chosen amongst the competent authorities and the Agency should examine the variation on behalf of other concerned authorities

Why Worksharing?

- Duplication in assessment of the same set of data is a waste of scarse resources
- Member states use each other assessment reports as basis for decision in Mutual recognition procedures and Decentralised procedures
- Consistent approach needed for products approved via national, mutual recognition and centralised procedures
- European agencies are part of a network; this network is strengthened by cooperation; benchmarking is instrument to build trust
- It is in the interest of public health (for patients and health professionals) to harmonise information for all products on the European market

Examples of Worksharing

- Radiopharmaceuticals (1990)
- Chemical variations (2005)
- PSUR assessment (2003)
- Paediatric data (2005)

Experience with Chemical-pharmaceutical variations

- Discussion on Worksharing for national approved products started in HMA, MRFG, QWP
- Situation complex because national chemical dossiers vary considerably however;
- 2 pilots for update dossier via Type II variation
- Coordination via BWP
- CMD(h) agreed in Worksharing procedure for minor change in packaging material affecting many products

Challenges in Worksharing

- Worksharing is only possible when submitted data are identical in all MSs; starting position and dossiers can be very different
- A formal procedures is needed – Can final decision be national?
- For communication mailboxes and network needed;
- Coordination of procedures at EU level is needed
- Implementation of Worksharing can be high administrative burden at national level
- Who has the mandate to discuss any scientific question?

Conditions to make Worksharing succesful

- Legal framework will facilitate the procedure
- Agreement needed on procedure before start
- Coordination at central point needed
- Tracking system needed to monitor procedures
- Transparency needed for all parties : Member States and industry
- Commitment needed from Member States to share the work
- National implementation should be simple administrative step- no reopening discussions
- Sufficient resources (fees)

Commission's proposal for Worksharing

CMDh has proposed to play coordinating role

- All Member States are represented in CMD(h)
- CMD(h) has mandate to discuss any regulatory, procedural and scientific question
- CMD(h) has experience in working with disharmonised dossiers
- CMD(h) has experience with Worksharing procedures MRP, DCP and others

Variation Regulation

Scope: Products in MRP/DCP and national?

Worksharing is on request MAH possible for
- minor variations Type IB
- Major variations Type II

- A group of variations (no extensions)

Of same MAH

Several marketing authorisations involved

Proposed procedure

- MAH shall submit all relevant authorities an application
- A reference authority shall issue an opinion on the valid application

Timetables

- *60 days Type IB or Type II*
- *210 days in case of line extensions*

National step: *30 days after final opinion, unless referral is initiated*

Referral procedures Variations

	Type IA	Type IB	Type II	CHMP referrals
2005	4044	1944	1509	7
2006	4524	2209	1916	
2007	5640	2298	2167	8

CMD(h) role in referrals

- For new applications 60 day referral procedure in CM(h) when Member State has raised Potential Serious Risk to Public Health (PSRPH)
- Under current legislation referrals for variations only to CHMP
- CMD(h) has proposed a similar 60 day referral procedure for variations only in sitations where one Member State has raised a PSRPH

Classification of Variations

Classification of variations

- Minor variation Type IA-*minimal impact on Q, S,E*
- Major variation Type II-*no extension and has signifcant impact on Q,S and E*
- Extensions- *a variation listed in the Annex*

- A variation which is not an extension and not classified

 - *by default Type IB*

Scientific recommendations

Recommendation on the classification of a Variation

On request by MAH

- By Coordination group
- Agency (EMEA) for centralised procedures

Agency and Coordination groups CMD(h) and CMD(v) shall cooperate

CMD(h) Working group on Variations is already existing

Simplification of administrative burden?(I)

MRP/DCP products

- A limited number of Member States is acting as RMS in 80-90% of Mutual Recognition procedures (MRP and DCP)
- Many RMSs are fully booked till 2008-2009
- The high number of variations is substantial amount of work of RMS
- Minor Type IA/IB variations are from an administrative point of view a burden for RMS and CMS (Tracking system, implementation decisions)
- Annual notification system can reduce administrative burden

Simplification of administrative burden?(II)

National products

- Worksharing can be particularly important to save resources at national level and for industry
- CMD(h) can coordinate procedures
- However there should be a fair balance:
- Worksharing for minor changes can create additional administrative burden (Type IA excluded)
- Main advantages when used for major changes
- Conditions should be taken into account

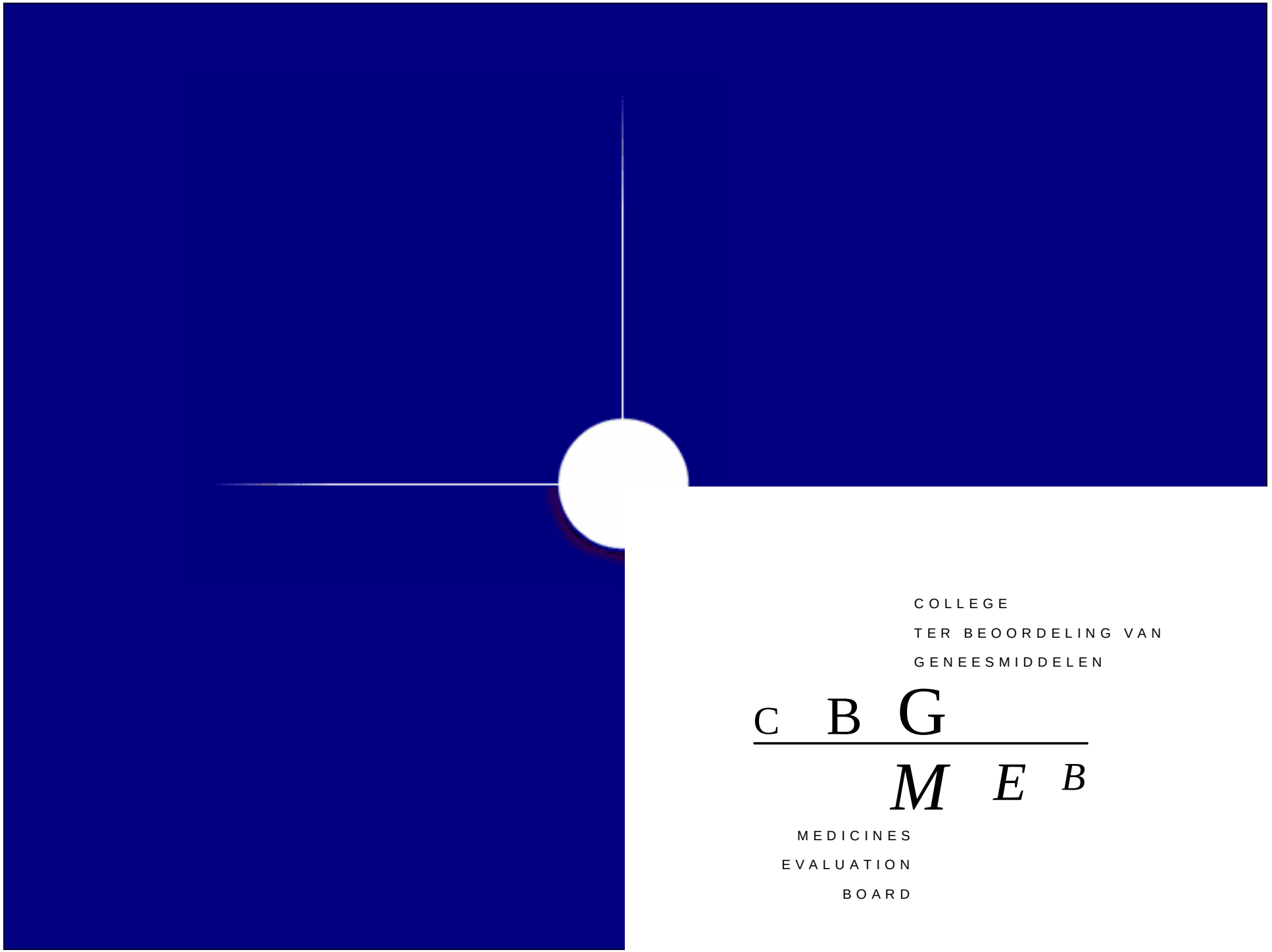
Conclusion

New Variations regulation will

- Harmonise and simplify European and national Variations
- Stimulate harmonisation in procedures and assessment of Variations
- Involve Coordination group in

- Organisation Worksharing
- Scientific recommendations
- Arbitration

Can reduce administrative burden if there is a strong commitment from Member State to accept role of a reference authority



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