CMDh
Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

BfArM
Federal Institute for Drugs and Medical Devices

14. DGRA Jahreskongress 2012: IV. Pharmakovigilance

Die Rolle des CMDh

31. Mai 2012

Wasserwerk Bonn

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The Coordination Group ...

... is a supranational body with a legal mandate laid down in Directive 2001/83/EC as amended

- ✓ a Members is the delegate of his MS (not of the NCA)
- ✓ EC is responsible for the Rules of Procedures
- ✓ EMA is responsible for the Secretariat

... but not a EMA-Committee

The Coordination Group – present mandate

Article 27

1. A coordination group shall be set up for the examination of any question relating to marketing authorisation of a medicinal product in two or more Member States in accordance with the procedures laid down in this Chapter. The Agency shall provide the secretariat of this coordination group.
2. The coordination group shall be composed of one representative per Member State appointed for a renewable period of three years. Members of the coordination group may arrange to be accompanied by experts.
3. The coordination group shall draw up its own Rules of Procedure, which shall enter into force after a favourable opinion has been given by the Commission. These Rules of Procedure shall be made public.

The amending legislation

31.12.2010 EN Official Journal of the European Union L 348/1

REGULATIONS

REGULATION (EU) No 1235/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 15 December 2010

amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products

L 348/74 EN Official Journal of the European Union 31.12.2010

DIRECTIVES

DIRECTIVE 2010/84/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 15 December 2010

amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use

New CMDh ?

- establish revised CMDh and define ist tasks and interaction with PRAC
  - amended Mandate
  - current Rules of Procedure to be amended

- clarification provided by EC
  - no need to reestablish the CMDh as the additional tasks due to the pharmacovigilance legislation is only an extention of the current mandate

The Coordination Group – future mandate – (1)

Article 27 (new)

1. A coordination group shall be set up for the following purposes:

   (a) the examination of any question relating to a marketing authorisation of a medicinal product in two or more Member States in accordance with the procedures laid down in Chapter 4;

   (b) the examination of questions related to the pharmacovigilance of medicinal products authorised by the Member States, in accordance with Articles 107c, 107e, 107g, 107k and 107q;

   (c) the examination of questions related to the modifications to the terms of marketing authorisations granted by the Member States, in accordance with Article 35(1).

The Coordination Group – future mandate – (2)

cont. ***Article 27(1) (new)***

The Agency shall provide the Secretariat of this coordination group.

For the fulfilment of its pharmacovigilance tasks including agreement and monitoring of risk management systems, the coordination group shall rely on the scientific assessment and the recommendations of the PRAC referred to in Article 56(1)(aa) of Regulation (EC) No 726/2004.

The Coordination Group – future mandate – (3)

2. The coordination group shall be composed of one representative per Member State appointed for a renewable period of three years. Members States may appoint an alternate for a renewable period of three years. Members of the coordination group may arrange to be accompanied by experts.

   Members of the coordination group and experts shall, for the fulfilment of their tasks, rely on the scientific and regulatory resources available to national marketing authorisation bodies. Each national competent authority shall monitor the level of expertise of the evaluations carried out and facilitate the activities of nominated coordination group members and experts.

The Coordination Group – future mandate – (4)

cont. ***Article 27(2)***

Article 63 of Regulation (EC) No 726/2004 shall apply to the coordination group as regards the transparency and independence of its members

3. The coordination group shall draw up its own Rules of Procedure, which shall enter into force after a favourable opinion has been given by the Commission. These Rules of Procedure shall be made public.

4. The Executive Director of the Agency or his representative and representatives of the Commission shall be entitled to attend all meetings of the coordination group.

The Coordination Group – future mandate – (5)

5. The members of the coordination group shall ensure that there is **appropriate coordination** between the tasks of that group and the work of national competent authorities, including the consultative bodies concerned with the marketing authorisation.

6. Save where otherwise provided for in this Directive, the Member States within the coordination group shall use their best endeavours to **reach a position by consensus** on the action to be taken. If such a consensus cannot be reached, the position of the **majority of the Member States** within the coordination group shall prevail.

7. Members of the coordination group shall be required, even after their duties have ceased, not to disclose information of the kind covered by the obligation of professional secrecy.

Binding CMDh majority vote…

"Save where otherwise provided for in this Directive, …" means not for

- authorisation procedures
  - new MA, EA
  - Type II Variation and Worksharing Procedure
  - Renewal
- PRAC Recommendations (majority with Commission Decision)

but for everthing else e.g. Validation and Procedures, Article 5 Recommendations, ...

Binding CMDh consensus to MS and MAH

with PRAC Recommendation

- consensus

  CMDh-Chair to inform MS and MAH on

  - action to be taken for the MA
    - maintain
    - vary
    - suspend
    - revoke
  - agreed timetable for implementation

  ➡ MS to **adopt** necessary measures

… implementation into the DE-AMG

„Die Ergänzung in Absatz 3 regelt, dass bei Entscheidungen der zuständigen Bundesoberbehörden, die sich auf einheitlich ergangene Empfehlungen der Koordinierungsgruppe stützen, eine Anhörung des Zulassungsinhabers grundsätzlich erforderlich ist, es sei denn Gefahr im Vorzug liegt vor. Allerdings bedarf es keines verwaltungsrechtlichen Vorverfahrens."

§ 30 Absatz 3 Satz 2 und 3:

„Das gilt auch, wenn eine Entscheidung der zuständigen Bundesoberbehörde über die Änderung der Zulassung, Auflagen zur Zulassung, den Widerruf, die Rücknahme oder das Ruhen der Zulassung auf einer **Einigung der Koordinierungsgruppe** nach Artikel 107g, 107k oder Artikel 107q der Richtlinie 2001/83/EG beruht. Ein Vorverfahren nach § 68 der Verwaltungsgerichtsordnung findet in den Fällen des Satzes 2 nicht statt."

→ kein Widerspruchsvefahren

Rules of Procedure

Composition

- One member per member state
  - EFTA states are fully associated
  - adequate regulatory and/or scientific expertise
  - delegated power from MS to express final opinions
- Alternates

Guarantees of Independence

- membership shall be made public
- professional qualification shall be specified
- to address any potential CoI

Voting Rules


... the tasks

General principle

- for MA authorised in more than one MS
  - Urgent Union Procedure (Article 107i)
  - PSUR (Article 107c and 107e)
  - PASS (PostAuthorisation Safety Studies)
  - PAES (PostAuthorisation Efficacy Studies)
- Coordination: Agency
- Evaluation: PRAC or MS (PSUR)
- Adoption
  - CHMP - if one central MA is included
  - CMDh – in all other cases

PSUR – (1)

- harmonised submission frequency
- Union reference date

  after consultation of the PRAC, by
- CHMP – if one central MA for the active substance is included
- CMDh – in all other cases

  publication by EMA followed by a variation to amend the PSUR frequency/date of the MA

  MAH may request CMDh/CHMP for a change of the PSUR frequency and/or union reference date

PSUR – (2)

- Initial Assessment
  - if central MA – Rapporteur appointed by PRAC
  - otherwise – MS appointed by CMDh
- Final Assessment/Recommendation by PRAC
- Adoption by
  - CHMP - if one central MA for the active substance is included

    Opinion, followed by a Decision of the European Commission
  - CMDh – in all other cases

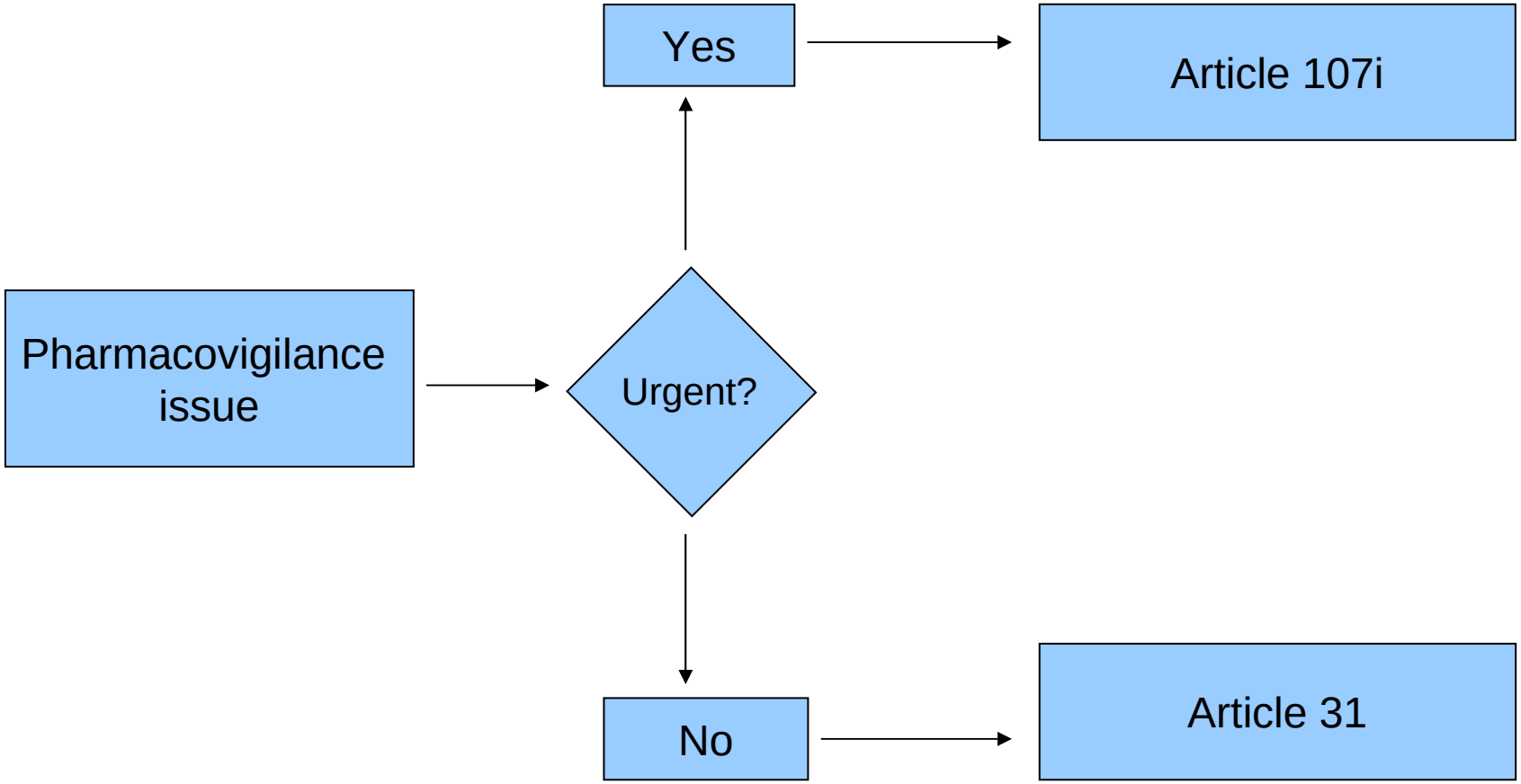
PSUR – (3)

But for national MA:

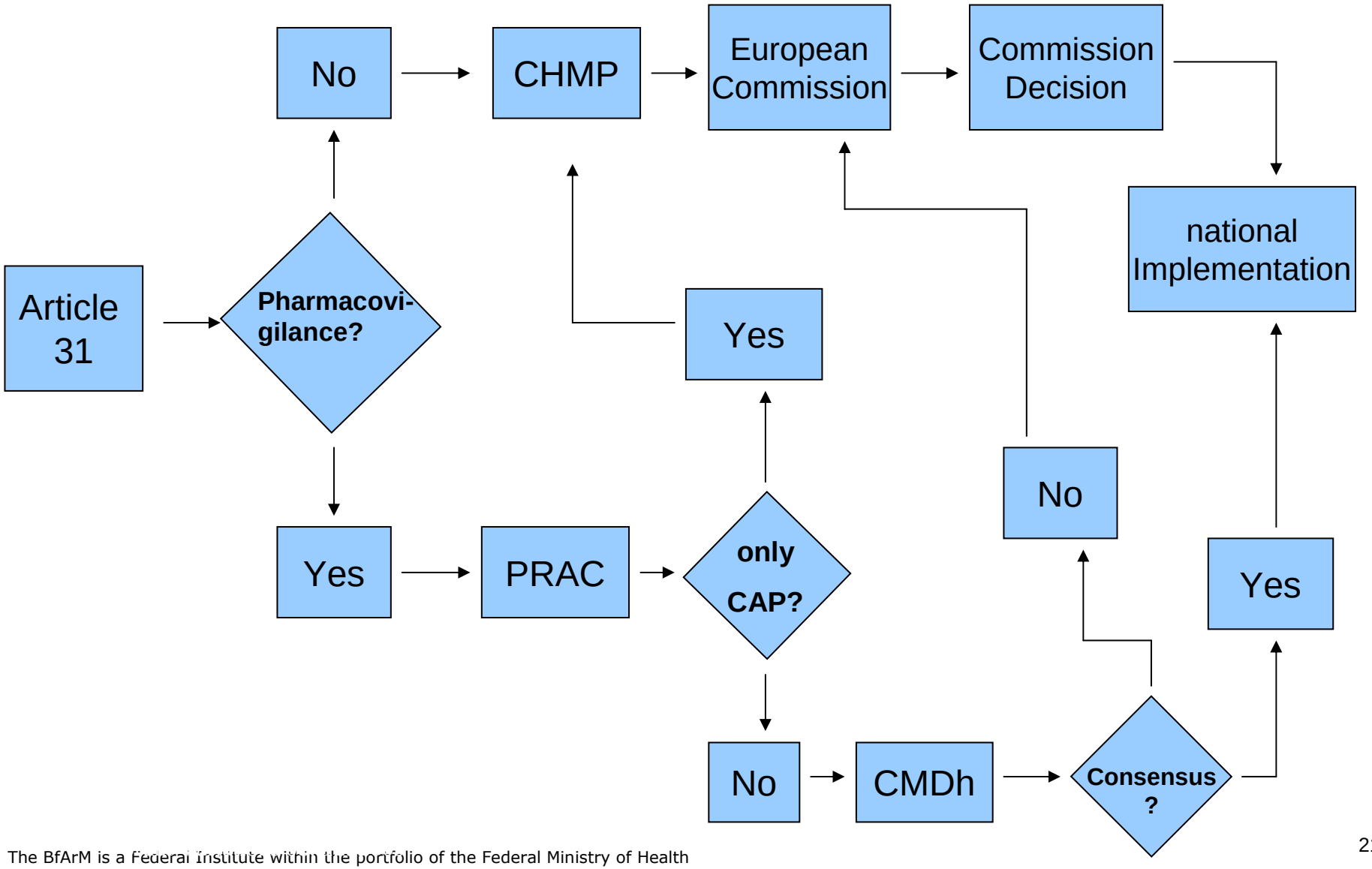
- Single PSUR Assessment is postphoned by EMA, due to
  - new EMA fee regulation not before 2014
  - EMA with resource/financial problems

- PSUR Worksharing (P-RMS)
  - existing are ongoing
  - new active substances to be taken on board?
  - outcome binding by CMDh position?

Pharmacovigilance issues …



Pharmacovigilance issues – (2)



Article 107 Referrals

Urgent Union Procedures – Article 107i, 107j and 107k

"… urgent action is considered necessary as a result of the evaluation of data resulting from pharmacovigilance activities"

- PRAC: 60 days to issue a recommendation, including wording in SmPC/PL if necessary and implementation timetable.
- CHMP/CMDh: 30 days to reach a position.

→ *tight time schedule: no clock-stop*

Cooperation PRAC - CMDh

- short timetables in Art 107 procedures (60 days)
- PRAC meets the second week before CMDh
- cooperation PRAC-CMDh starts at national level in the MS, members should work as a team
- CMDh could appoint a coordinator at start of procedure to inform CMDh

Article 107i and Variations ?

- Art 107i shall be initiated by MS or Commission in any of the following cases:
  a) it considers suspending or revoking a marketing authorisation
  b) it considers prohibiting the supply of a medicinal product
  c) it considers refusing the renewal of a marketing authorisation

  (*! interaction with Article 29-Referrals at the CMDh !*)
  d) is informed by MAH that, on the basis of safety recommendations, he has interrupted the placing on the market,.
  e) it considers that a new contraindication, a reduction in dose, or a restriction in indications is necessary

Role of USR and Safety Type II variations ?

Article 107i ?

Bildung von unlöslichen Partikeln bei carboplatinhaltigen Arzneimitteln

Erstellt: 16.05.2012 **Aktualisiert:** 16.05.2012

Bei Konzentraten zur Herstellung von Infusionslösungen mit dem Inhaltsstoff Carboplatin kann es innerhalb der Laufzeit zur Bildung von unlöslichen, kristallinen Partikeln kommen. Betroffen sind Konzentrate zahlreicher pharmazeutischer Unternehmer. Die durchgeführten Untersuchungen haben ergeben, dass es sich bei den Partikeln um substanzspezifische Auskristallisationen des Wirkstoffs handelt. Trotz dieser Ausfällungen liegt der Wirkstoffgehalt weiterhin innerhalb der Produktspezifikationen. Bisher sind dem Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) keine Nebenwirkungen im Zusammenhang mit den Carboplatinpräzipitaten gemeldet worden, zumindest mittel- und langfristige Risiken können jedoch nicht ausgeschlossen werden.

Präparate der folgenden pharmazeutischen Unternehmen waren von Ausfällungen betroffen, so dass die belasteten Chargen vom Markt zurückgerufen wurden: Actavis Group PTC ehf, Axios Pharma GmbH, EBEWE Pharma GmbH Nfg. KG, Haemato Pharm AG, Hexal AG, Hikma Farmaceutica S.A., Lapharm GmbH, Medac Gesellschaft für klinische Spezialpräparate mbH, Medicopharm AG, NeoCorp GmbH, Onkovis GmbH und Sandoz Pharmaceuticals GmbH.

Zwei pharmazeutische Unternehmen - Accord Healthcare Ltd. und Hospira Deutschland GmbH - haben dem BfArM bisher nicht alle geforderten Untersuchungsergebnisse vorgelegt.

Das BfArM hat folgende Maßnahmen veranlasst und die zuständigen Landesbehörden entsprechend informiert:

... other pharmacovigilance items

… for marketing authorisations

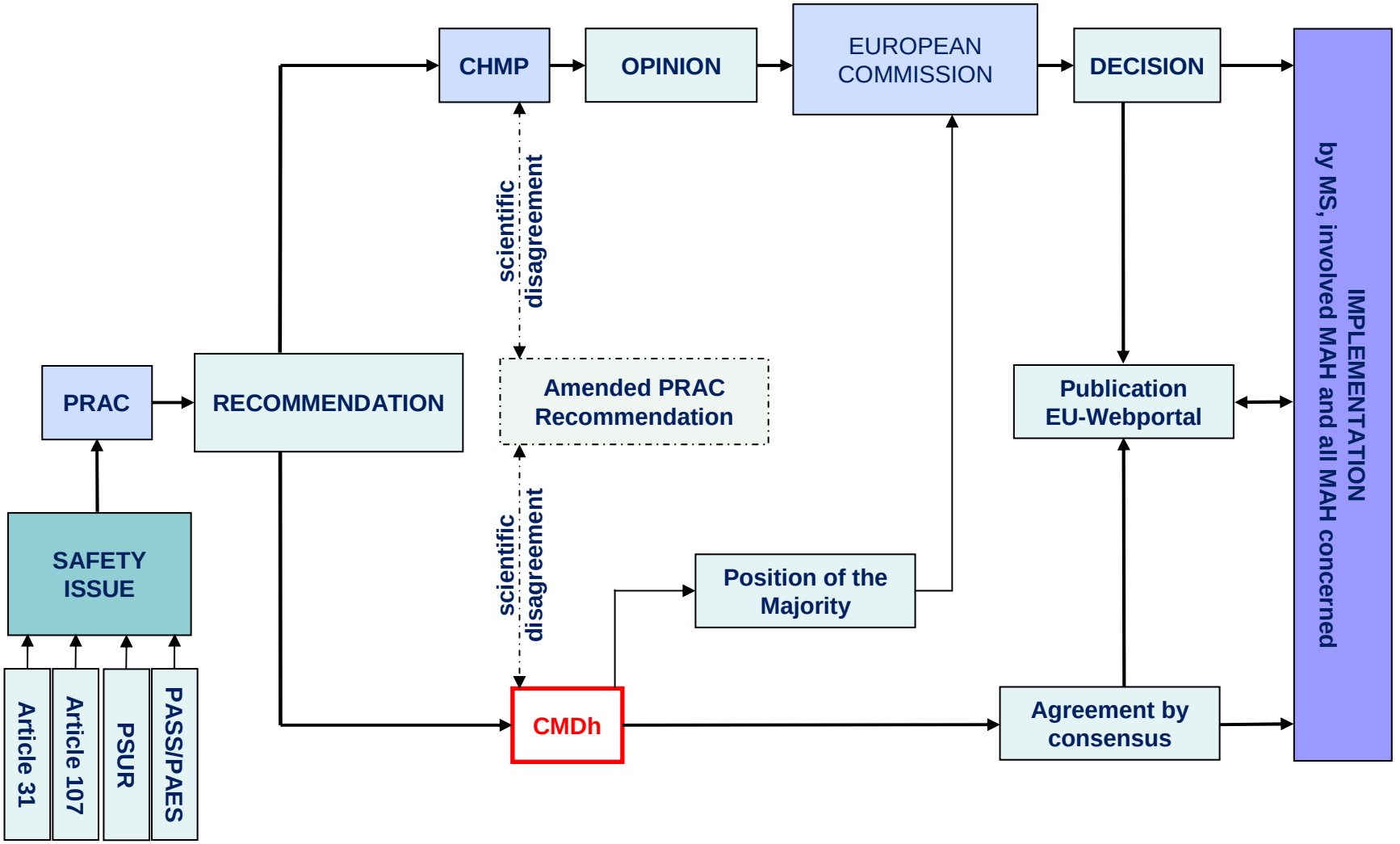
- **Risk Management System**

  The CMDh will approve risk management systems and **monitor their effectiveness**.

- **PASS and PAES**

  legal basis for a condition to the MA

Role of CMDh in EU decision making



slide from Ms. Popova – BDA (amended)

European Medicines Web-Portal

- Article 22 Directive

  "The marketing authorisation holder shall ensure that the product information is kept up to date with the current scientific knowledge, including the ***conclusions*** *of the assessment and recommendations* ***made public*** *by means of the European medicines web-portal established in accordance with Article 26 of Regulation (EC) No 726/2004."*

- a MA may be suspended, revoked or varied if the particulars have not been amended or conditions have not been fulfilled

The 'revised' Coordination Group ...

... is still a supranational body but with an extended legal mandate laid down in Directive 2001/83/EC as amended

- ✓ a Members is the delegate of his MS, but independent and transparent according to the rules of a EMA-Committee member
- ✓ EC is responsible for the Rules of Procedures
- ✓ EMA is responsible for the secretariat

... is still not an EMA-Committee, but certain rules of an EMA-Committee will apply

... and direct interaction with EMA


Federal Institute for Drugs
and Medical Devices (BfArM)
... many thanks
for your kind attention
The BfArM is a Federal Institute within the portfolio of the Federal Ministry of Health