Réunion d'information
Informatievergadering

11/12/2009

Inleiding

Annemie Decostere

Adviseur Volksgezondheid pharma.be

Programme

Introduction

Plan d'action pour le traitement accéléré des dossiers d'enregistrement et pour remédier au Backlog

- **Présentations**
- **Q&A**

Pause café

Implémentation nationale du nouveau variations Regulation (EC/1234/2008)

- **Présentations**
- **Q&A**

Clôture

Programme: première partie

Plan d'action pour le traitement accéléré des dossiers d'enregistrement et pour remédier au Backlog (AFMPS)

Présentations (45 min)

Indicateurs (Vanessa Binamé)

Action 1: Withdrawal letter (Vanessa Binamé)

Action 2: Implémentation des "referrals", "class labellings" et d'autres décisions/recommandations européennes (Valérie Lescrainier)

Action 4: Clôture des dossiers sans impact sur le AMM light (Iris Geussens)

Action 5: Evaluation complète du RCP, de la notice et de l'étiquetage dans le cadre de la procédure scientifique (Christelle Beeckmans)

Action 6: Législation pour retrait des dossiers inactivés (Vanessa Binamé)

Action 7: Analyse de risque des dossiers constituant l'arriéré en phase d'évaluation, test de lisibilité et worksharing (Wim Penninckx)

Action 8: Autocontrôle (Wim Penninckx)

Questions and answers (45 min)

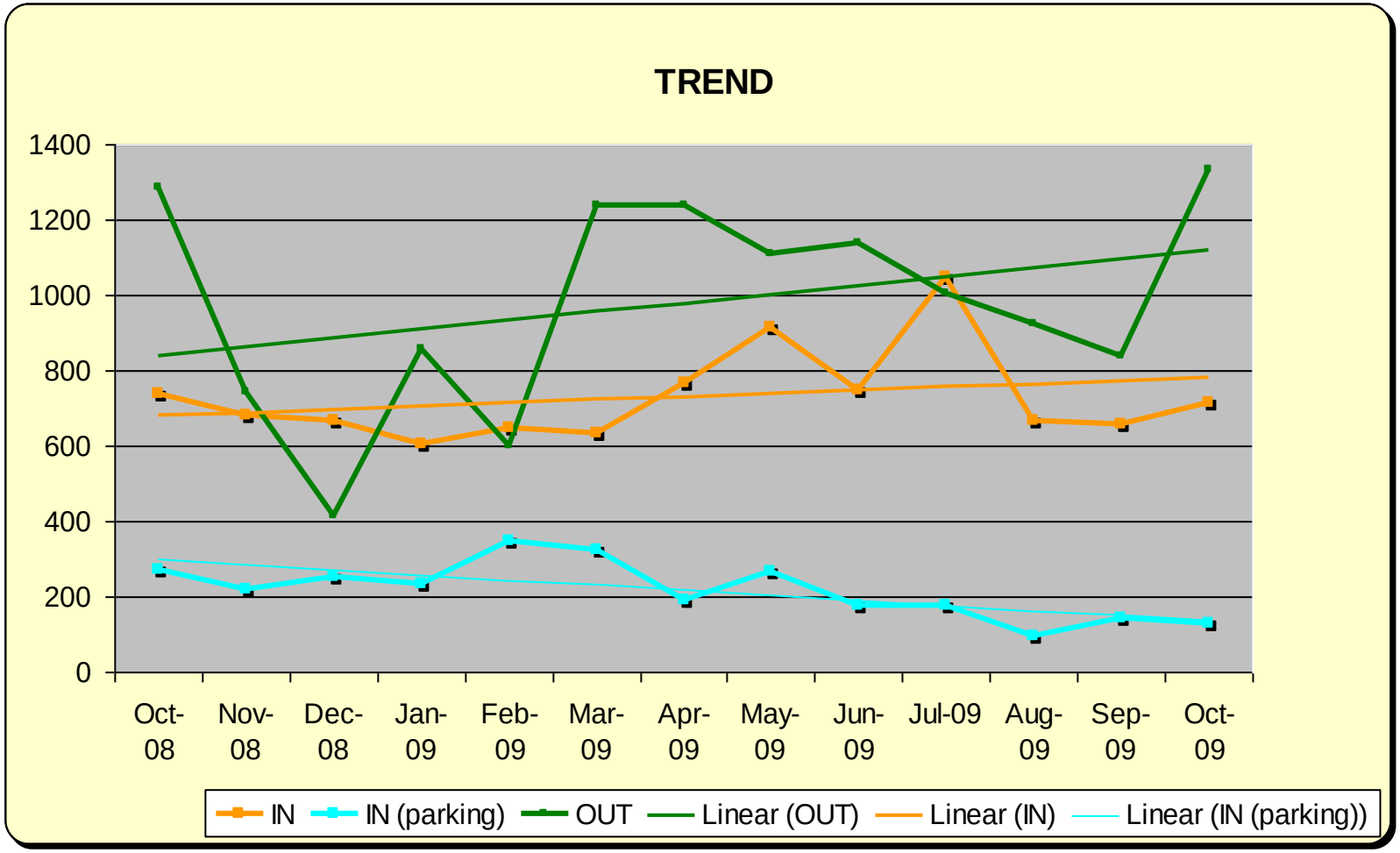
Federal **A**gency for **M**edicines and **H**ealth **P**roducts (FAMHP)

Global KPIs

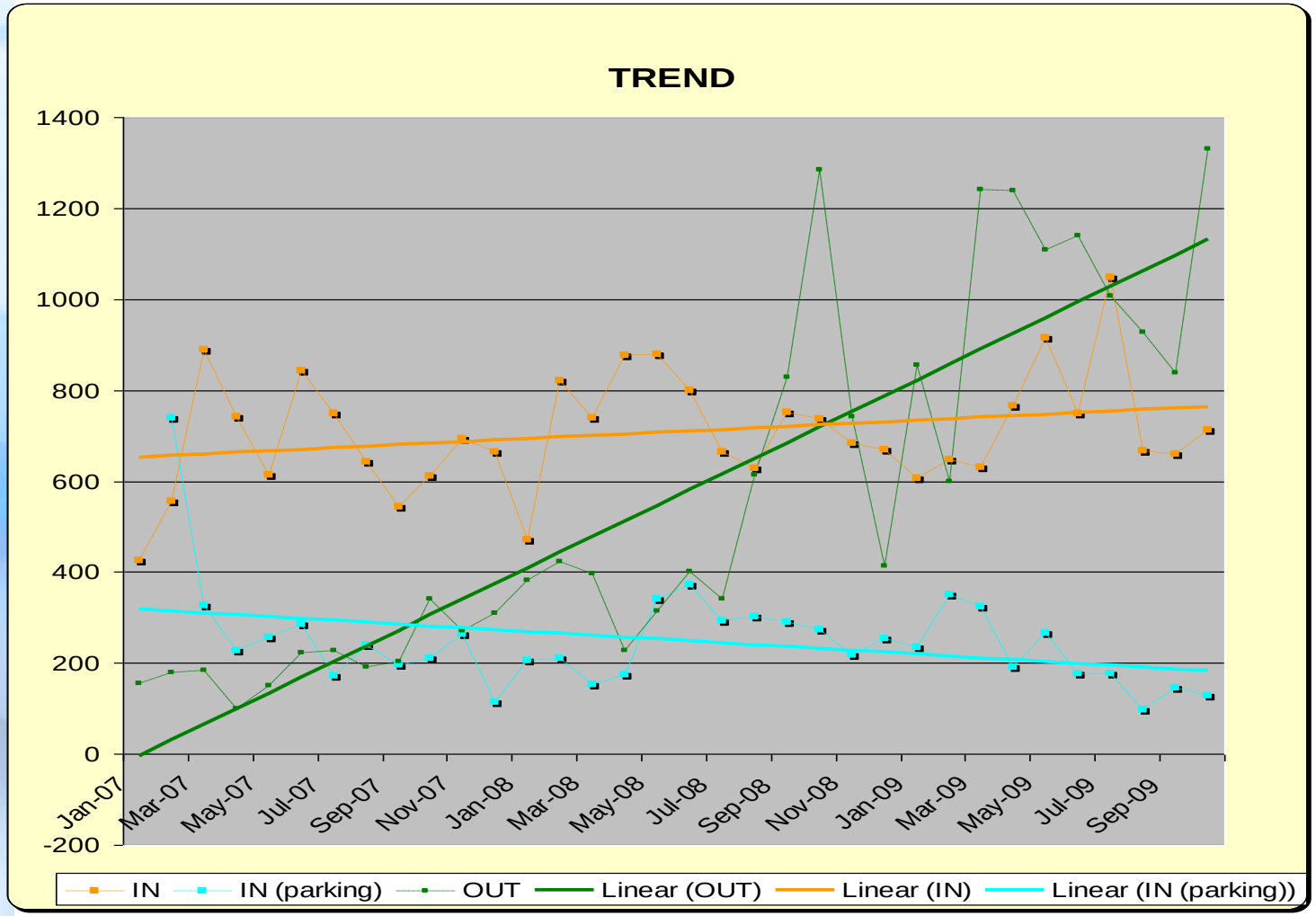
Vanessa Binamé

11/12/2009

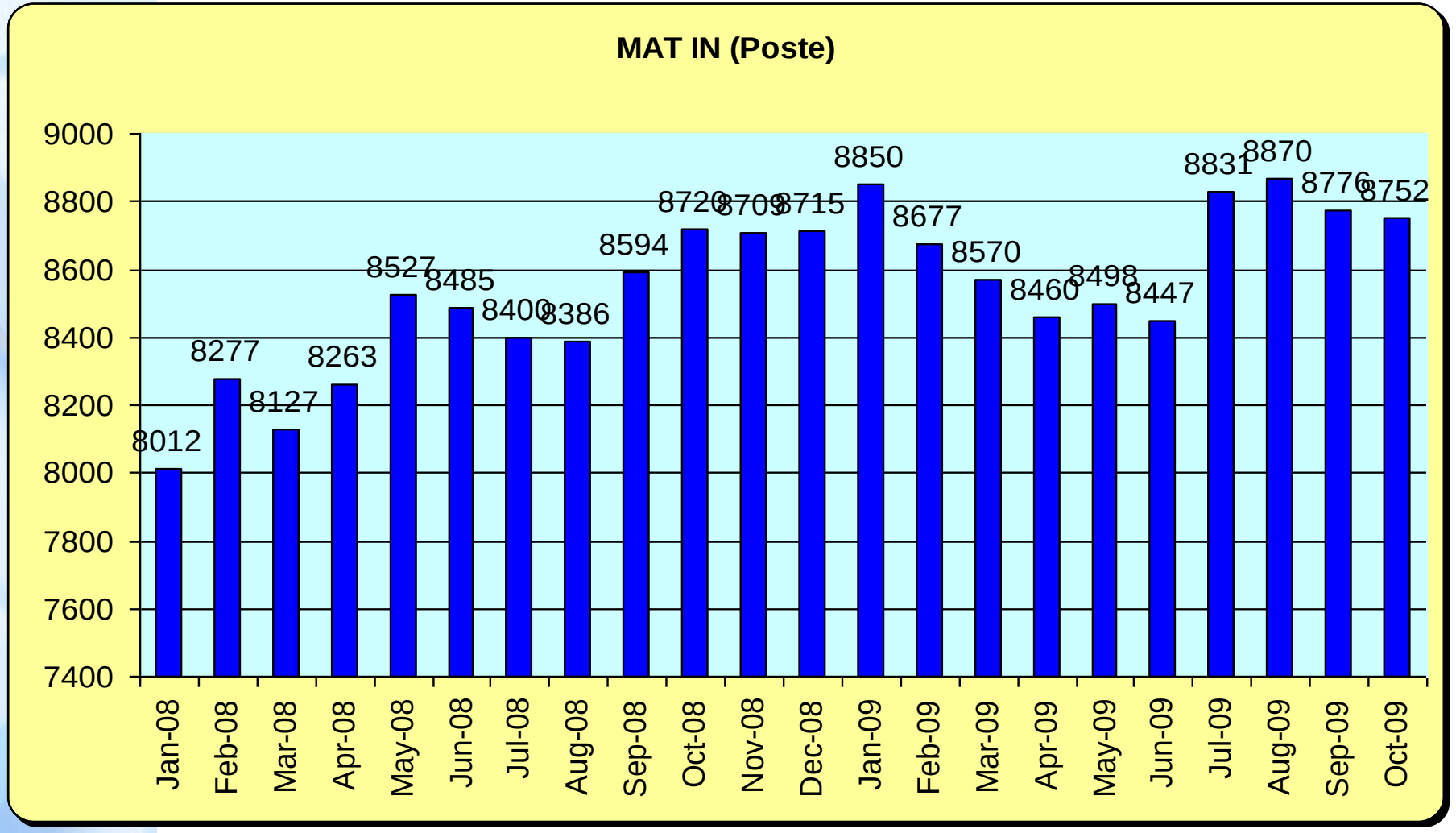
IN / OUT - Trend between 10/08 and 10/09



IN / OUT - Trend since January 2007



MAT IN FROM JANUARY 2008



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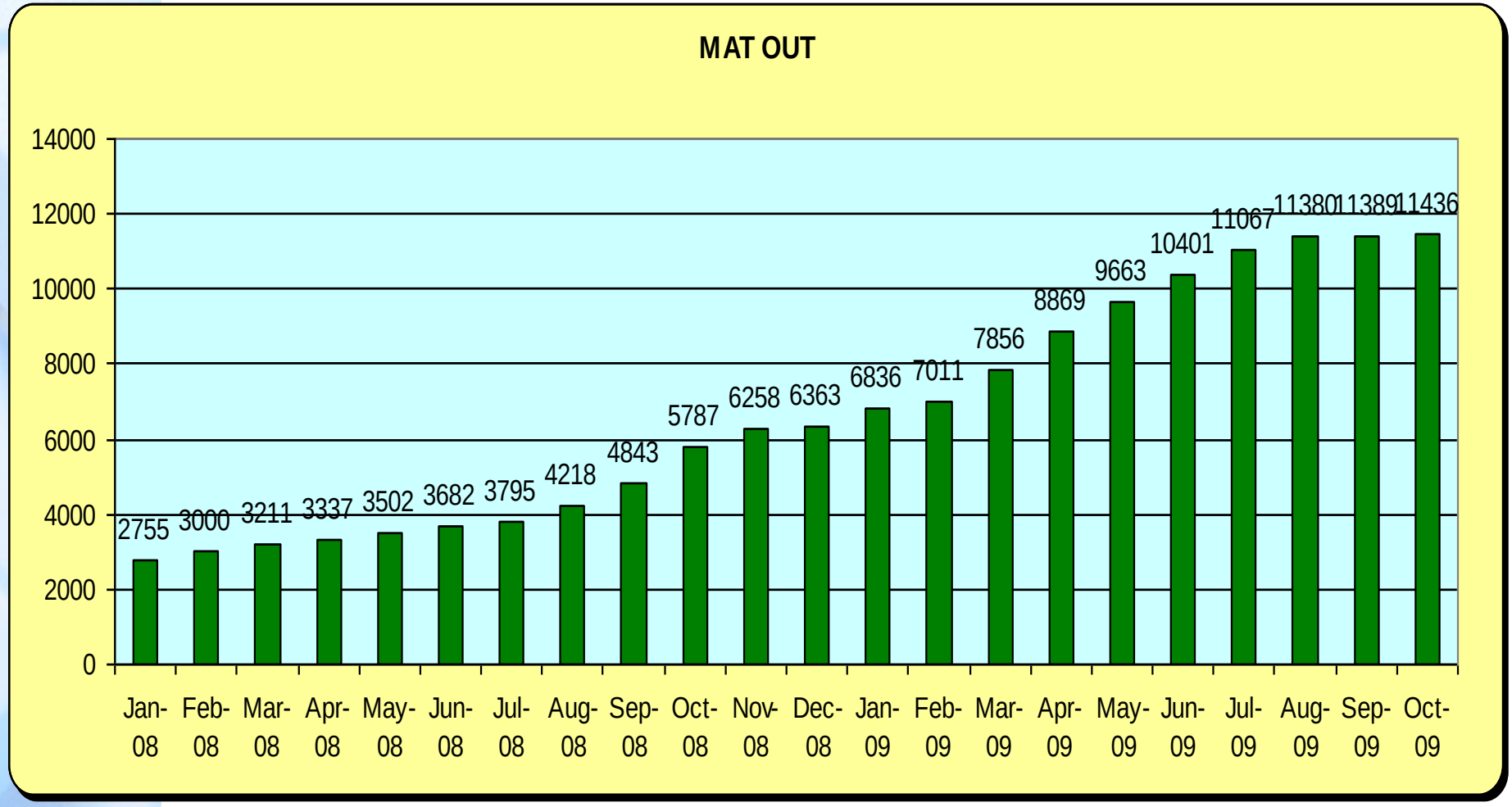
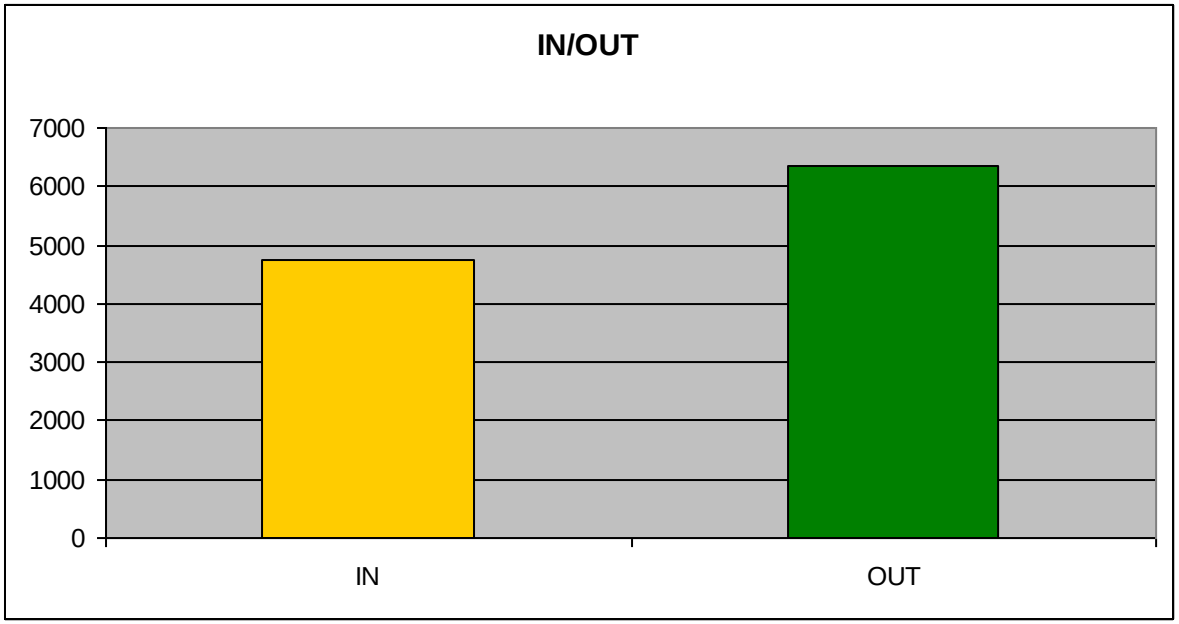
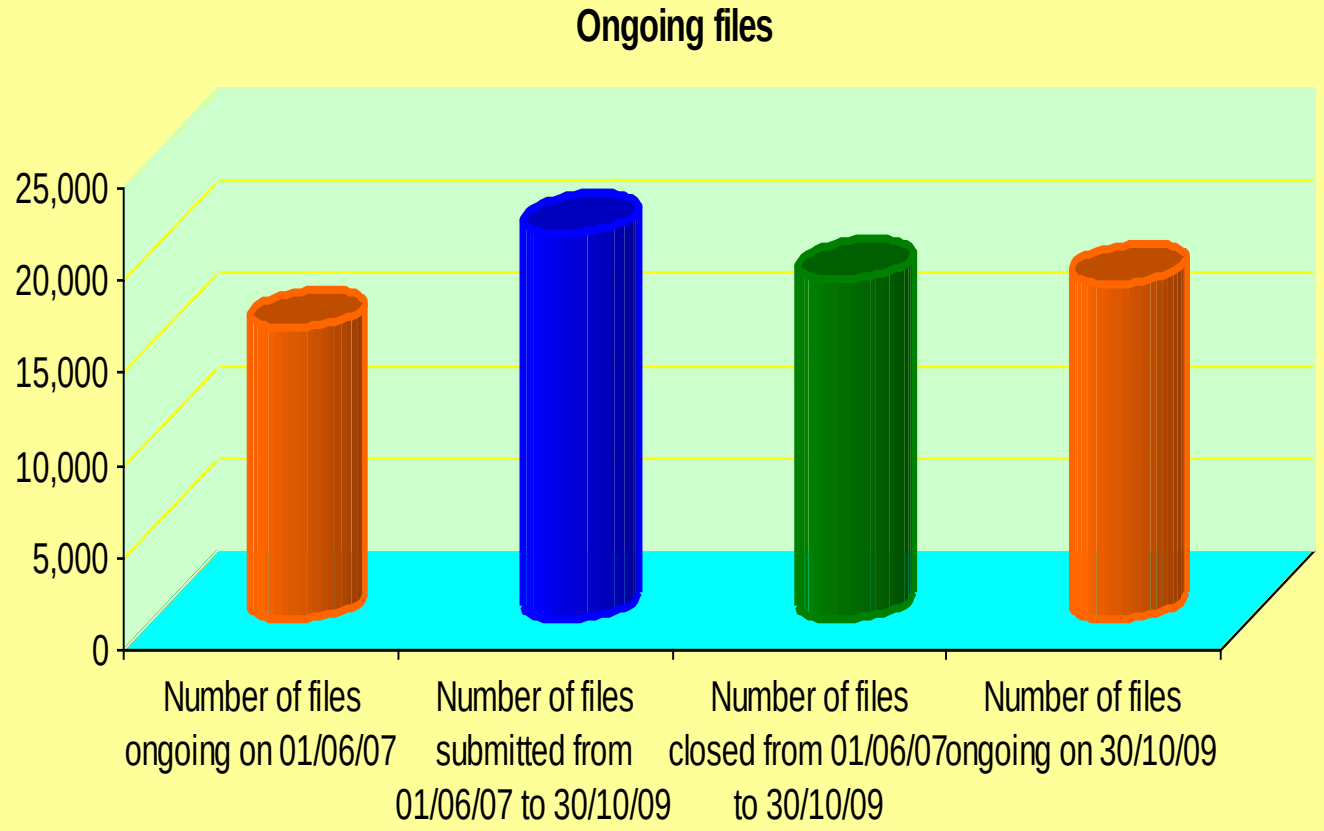


IN / OUT from May 2009 (6 months)



IN / OUT from January 2008



Federal **A**gency for **M**edicines and **H**ealth **P**roducts
(FAMHP)

Action 1: Withdrawal letter

Vanessa Binamé

11/12/2009

Action 1: Withdrawal Letter

Number of files withdrawn since 01/07/09: 15

No impact on the Backlog

No return from the actions put in place

- Withdrawal letter template
- General mailbox withdrawalletter@afmps.be

For the future, the list of the files and medicinal products concerned can be placed in an annex to the withdrawal letter => only one withdrawal letter by MAH

Action 1: Withdrawal Letter

FAMHP is currently reviewing if there are still files open for medicinal products withdrawn between 2005 and 2008. These files will be closed progressively. Until now, 63 files for medicinal products withdrawn have been closed

Is it possible to link this exercice with the open files of 2006 and the dossiers considered with non priority?

Agence **F**édérale des **M**édicaments et des **P**roduits de **S**anté
(AFMPS)

Implementation of Referrals/Recommendations

Valérie Lescrainier

11.12.2009

Implementation of referrals/recommendations

- Scope
- Links
- Deadlines
- Internal Procedure
  - Before submission
  - Process
    - Full update SPC/PIL/labelling
    - No full harmonisation
    - Dossier not received

Implementation of referrals/recommendations

Scope:

- Art.30 referral
- Art.31(1)/31(2) referral
- Art.29 under the paediatric regulation 1901/2006/EC
- Specific recommendations (following article 45 or article 46 worksharing)
- Pharmacovigilance recommendations

Implementation of referrals/recommendations

- Art.30 referral (= Divergent Decision Referral)
  - → SPC/PIL/labelling harmonization
    - → texts translations in Annex of the decision

- Art.31(1)/31(2) referral (= Community Interest Referral)
  - → art.31(1): complete SPC is affected
  - → art.31(2): specific parts of the SPC are affected; concerns a range of MPs or a therapeutic class. MA issued nationally will remain national.
    - → texts translations in Annex of the decision

Implementation of referrals/recommendations

For MA issued nationally, MAH has to choose an RMS for all up-coming procedures (except for referral based on Article 31(2))

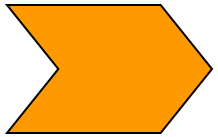
→ implementation is the last national variation

- Art 29 under the paediatric regulation

→ new indications, including paediatric indications

or → a new pharmaceutical form

or → a new route of administration



Choose RMS!

Implementation of referrals/recommendations

- Specific recommendations following art 45 or 46 worksharing

➢ article 45: paediatric studies already completed by 26/01/2007

➢ article 46: paediatric studies completed after 26/01/2007

- Pharmacovigilance Working Party recommendations

→ texts translation are not published by CMDh!

Implementation of referrals/recommendations

Links

Referrals and art 29 paed.reg.:
http://ec.europa.eu/enterprise/pharmaceuticals/register/refh_others.htm

Recommendations:
http://www.hma.eu/23.html

Implementation of referrals/recommendations

Links

Classification guidance on minor variations of type IA, minor variations of type IB and major variations of type II

http://ec.europa.eu/enterprise/sectors/pharmaceuticals/better-regulation-variations-regulations-developments_en.htm

CMDh Press release:

http://www.hma.eu/249.html

Implementation of referrals/recommendations

Deadlines:

Implementation of referrals:

→ 30 days after publication for products included in the annex of the Commission Decision

→ 90 days for essentially similar products

Implementation of specific recommendations:

→ 90 days after publication

Implementation of Pharmacovigilance recommendations:

→ specific time-table for each recommendation

Implementation of referrals/recommendations

Actual situation

	Art.30	Art.31(1) 31(2)	Art.29	Recommendations
Nat.Reg	NAT II variation	NAT II variation	NAT II variation	NAT II variation
Nat.Reg ess. Sim.				
MRP/DCP Reg	NAT II variation	NAT II variation	MRP II variation	MRP II variation
MRP/DCP Reg; ess. Sim.	MRP IB 46 (if <90 days)	NAT II variation	MRP II variation	MRP II variation

Letter from the FAMPH

Implementation of referrals/recommendations

From January 1st 2010

	Art.30	Art.31(1) 31(2)	Art.29	Recommendations
Nat.Reg	NAT IA IN (C.I.1)	NAT IA IN (C.I.1)	NAT II Variation (30 days)	NAT IB (C.I.3)
Nat.Reg ess. Sim.	NAT IB (C.I.1)	NAT IB (C.I.1)		
MRP/DCP Reg	MRP IA IN (C.I.1)	MRP IA IN (C.I.1)	MRP II Variation (30 days)	MRP IB (C.I.3)
MRP/DCP Reg; ess. Sim.	MRP IB (C.I.1)	MRP IB (C.I.1)		

Letter from the FAMPH

Implementation of referrals/recommendations

Internal procedure

- **Before Submission:**
  - FAMPH letter with clear instructions
  - (except for MRP procedures)
    - dossier requirements
    - deadlines for introduction
      - 10 days for referrals
      - 30 days for recommendations
    - links to texts to be implemented in each national language

Implementation of referrals/recommendations

For recommendations, texts will be translated in French and Dutch by the FAMPH (links to our website will be mentioned in the letter). Translation in German will be the responsability of the MAH.

- **Process:**
  - 2 separate ways
    - Full update SPC/PIL/labelling
    - No full harmonisation SPC/PIL/labelling

Implementation of referrals/recommendations

1. **Full update SPC/PIL/Labelling**
   - Art.30, 31(1), art. 29 paed.reg.
     (new pharmaceutical form/new route of administration)
   - Parallel national/MRP implementation art.30 for essentialy similar products

→ **full flow with high priority**

Cluster

+ pending clinical variations

+ variations/renewals that can be finalized

Outcome : new MAD, SPC/PIL/labelling

Implementation of referrals/recommendations

2. No full update SPC/PIL/Labelling

- Art.31(2), art. 29 paed.reg. (new indication)
- Recommendations

→ **simplified flow**

No cluster!

Outcome : approval letter which includes the *approved section(s)* for SPC/PIL.
No new MAD, SPC/PIL!

Implementation of referrals/recommendations

3. Dossier not received

Letter for suspension with inactivation of pending dossiers for same MAD

Implementation of referrals/recommendations

Procedure type	Letter FAMPH	Submission date	Closing date
referral art 29	16/11/2009	19/11/2009	03/12/2009
Paediatric recomm.	03/08/2009	11/09/2009	04/12/2009
Paediatric recomm.	03/08/2009	01/12/2009	04/12/2009
Paediatric recomm.	17/11/2009	27/11/2009	04/12/2009
Paediatric recomm.	17/11/2009	25/11/2009	07/12/2009
Paediatric recomm.	17/11/2009	27/11/2009	07/12/2009
Paediatric recomm.	17/11/2009	27/11/2009	07/12/2009

Many thanks for your attention!

Federal **A**gency for **M**edicines and **H**ealth **P**roducts
(FAMHP)

Backlog actionplan
Variations without impact on light AMM

Iris Geussens
DG Post Authorisation, Head of Division a.i.

11.12.2009

Variations without impact on light AMM

Scope of the project:

- Changes with no effect on:
  → AMM
  → SPC and PIL
  → labelling

- Type of dossiers
  → Backlog: NP IA-IB, MRP CMS IA-IB, MRP CMS II ana
  → new introduced dossiers (from 1/6/09):
  same as backlog + NP II ana

Variations without impact on light AMM

Process of the project:

Backlog dossiers:

- Team of 2 persons
- Only closing of the dossiers

New introduced dossiers:

- Team of 6 persons
- Whole cycle “upload-validation-dossier management-closing” → one dedicated person
- If assessment needed → second person involved
- Simplified way in MeSeA

Variations without impact on light AMM

Closing phase

- Most important: automatic mail → implementation (except when additional MA)
- Update of variation table, but not sent to applicant
- Dossier closed in MeSeA

Variations without impact on light AMM

results

Variations without impact on light AMM

results

- Total In from july 2009: 1984
- Total out from july 2009: 2178
- Of total closed: 926 dossiers Backlog
- Total of new dossiers yet not closed: 532
- Reasons why not yet closed:
  → timetable not yet finished: mainly type II ana
  → dossier not yet paid
  → dossier incomplete: invalid

Variations without impact on light AMM

Conclusions:

Efficient project that
now can be standard procedure.

Variations without impact on light AMM

Impact Better Regulation:

- Grouping: one variation with impact → out of scope of this procedure.
- Possible diminuation of dossiers faling into the scope → possibility to adapt scope.

Variations without impact on light AMM

Thank you for your attention!!!

Federal **A**gency for **M**edicines and **H**ealth **P**roducts
(FAMHP)

Full evaluation of the SPC, PL and labelling during the procedure

Christelle Beeckmans

11/12/2009

Objective

Reminder

The examination of the SPC, PL, labelling, mock-up (3 languages) and the logo

⇨ by the dossier manager

⇨ during the evaluation phase

Live in 15/09/2009

Procedure applicable for

- New applications NAT
- New applications DCP and MRP as CMS
- type II clin variations NAT
- New applications, type II clin variations and RQ - DCP and MRP as RMS

NOT for

- variations and RQ – DCP and MRP as CMS
- other variations and RQ NAT

Focus on

Reminder

- QRD template
- Standard terms of pharmaceutical form, route of administration and special precautions for storage

  + correct terminology
- Full naming of the medicinal product
- Similarity between the documents about

  - Registration number
  - MAH
  - …

Focus on (2)

- Common leaflets for medicinal products

  with same umbrella name, MAH, active substance, legal basis
- Other modifications noticed out of the topic of the variation
- Blue box requirements
- Granted derogations
- Delivery modus

Examples

Extract from reporting of November 09

- Standard terms:
  - -administration intraveineuse → voie intraveineuse
  - -flacon → fles
  - -dispergeerbare tablet → dispergeerbare tabletten
- Registration number:
  - -to adapt registration numbers to the unique registration numbers
- Other modifications noticed:
  - -the blisters only authorized but in the SPC the bottles mentioned too.
  - -to adapt the contents of the PIL to the changed contents of the SPC

Sending to the applicant

A completed check list is annexed to

For DCP and MRP with BE as RMS of CMS

⇨ the letter of comments

For NAT

⇨ the letter of deficiency of the Belgian Commission

The content of the check list changes according to the type of procedure

Translation of approved SPC,PL and Labelling

Documents Sent

- For NAT

⇨ after the notification of approval by the Belgian Commission i.e. after mail 'round up'

For DCP and MRP

⇨ within 5 days after the notification of approval of the RMS

- To fagg_closing_file@fagg.be + declaration of conformity of translations

KPI

- Number of dossiers with evaluation of SPC,PL and labelling during the evaluation phase

- Number of dossiers with evaluation of SPC,PL and labelling during the closing phase

- Quality of SPC, PL and labelling : type of comments made during the evaluation and the closing phase

Thanks a lot

For your attention

Federal **A**gency for **M**edicines and **H**ealth **P**roducts
(FAMHP)

Inactivation – legal basis

Vanessa Binamé

11/12/2009

Action 6: Legislation for inactivation

Amendment to the Law (25/03/1964) should be published in January

Next step: amendment to the Royal Decree (14/12/2006)

Text ready and discussed with the Industry representatives

Action 6: Legislation for inactivation

MAH has to submit the documentation necessary for the closing of his file within the 24 weeks from the 1st request of FAMHP

FAMHP works during 6 weeks on the file (2+2+2). If no answer or incomplete answer, no additional reminder after this period

If at the end of the 18 weeks still no answer or incomplete answer, the file is automatically withdrawn

Action 6: Legislation for inactivation

Consequence

A new application has to be submitted

Exception: MRP Variation

administrative file to update the MA accoding to the approved variation should be submitted before the next variation in order to maintain the life cycle of the medicinal product

As soon as the new legislation will be published, all files already inactivated will also profit of a new period of 24 months

Federal Agency for Medicines and Health Products
(FAMHP)

Action plan backlog during evaluation phase

Wim Penninckx
Evaluators, *division head a.i.*

11.12.2009

Content

I. New applications & type II variations
(Evaluator's division, DG PRE)

- I.1. Objectives
- I.2. Implemented action plan
- I.3. Current status
- I.4. Further plans quality assessment

II. Renewals
(Vigilance division, DG POST)

I.1. Objectives

- Elimination of backlog of national dossiers at evaluator's division by the end of 2010.
- To prevent creation of new backlog by incoming dossiers.
- To identify risk factors for the future.

I.2. Implemented action plan

- Significant reduction of time attributed to dossiers where Belgium is CMS in DCP/MRP

  (*selection of dossiers based on risk analysis).*
- Significant reduction in number of dossiers where we are candidate RMS in DCP/MRP.
- Reduction of redactional effort for assessment reports.
- Clinical: additional junior assessor (temporary contract)
- Quality: transfer of type IB variations to DG POST

I.2. Implemented action plan

- Type II variations arising from readability testing on marketed products:

Selection of dossiers that are assessed.

Scientific criteria

e.g.
- risk profile product
- manipulation risk

Procedural criteria

e.g.
- Product not on market.
- Generic (readability testing performed on reference product).
- Product more than 25 years on market without problems.

I.2. Implemented action plan

- Call centre priorities:
  - ✓ No new call centre priorities accepted for assessors
  - ✓ Where a call centre priority "gestion" was accepted before:

    Handled with priority as far as compatible with backlog action plan.

- Continuous monitoring of the backlog reduction.

I.3. Current status: *Clinical assessors*

- 250 dossiers waiting for assessment in July 2009
- monthly input of 15 new national dossiers that require clinical assessment (new applications & type II variations)

↓

Target output

= 40 reports for national dossiers per month

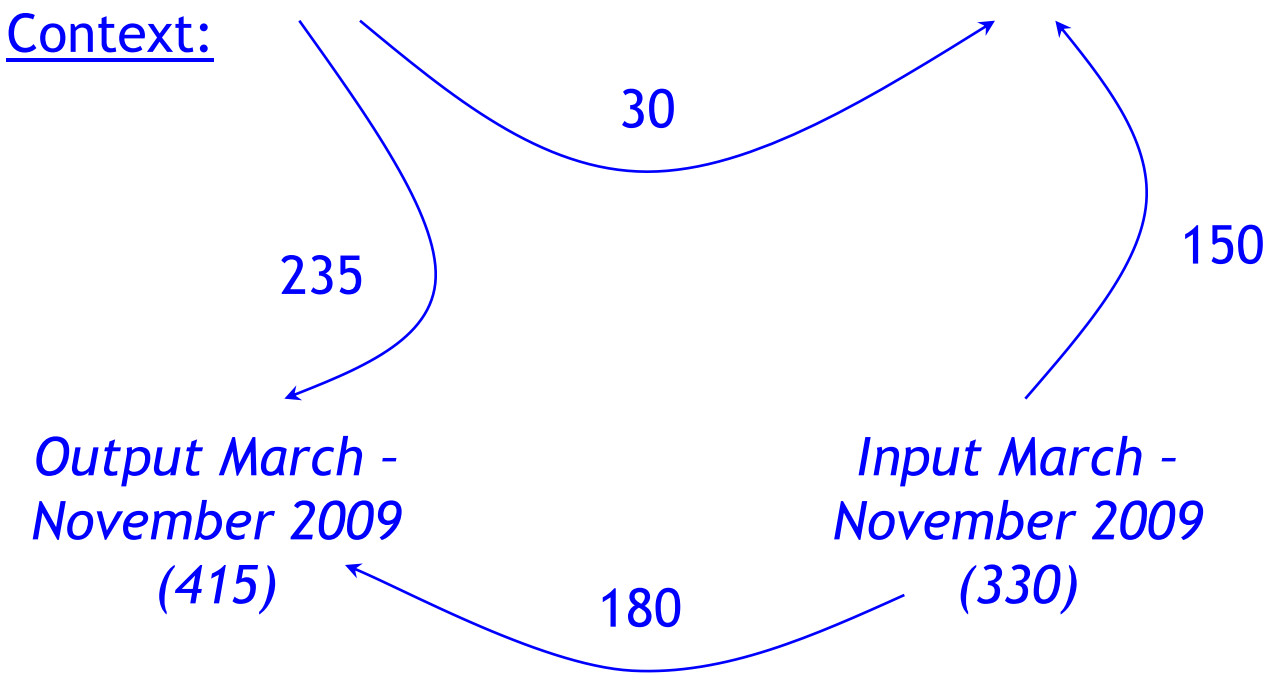
↓

Results for August, September and October 2009:

in line with objective

I.3. Current status: *Quality assessors*

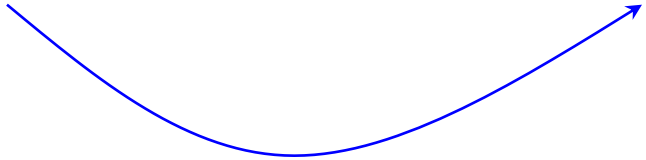
Dossiers waiting for assessment	
March 2009:	*November 2009:*
265	180



I.3. Current status: *Quality assessors*

Dossiers waiting for assessment

March 2009:	*November 2009:*
265	180



Reduction not considered sufficient to guarantee elimination of analytical backlog by the end of 2010

Additional measures needed

I.4. Further plans (quality assessment)

(a). MRP-like procedure national variations to module 3

- Recognition of assessment with positive advice performed by other MS for the same variations.
- In operation from 15/12/2009.
- Full description of procedure published on website of FAMHP.

I.4. Further plans (quality assessment)

(a). MRP-like procedure national variations to module 3

- Two options to document positive assessment by other MS:

  i). Assessment report of other MS

  ii). Expert report by QP or Regulatory Affairs Manager on the regulatory steps during procedure in other MS
  + copy questions / responses

I.4. Further plans (quality assessment)

(a). MRP-like procedure national variations to module 3

- New submission national type II applications
  - ✓ Request for MRP-like procedure should be clearly indicated in cover letter and application form.
  - ✓ Additional documentation in annex to application form.

I.4. Further plans (quality assessment)

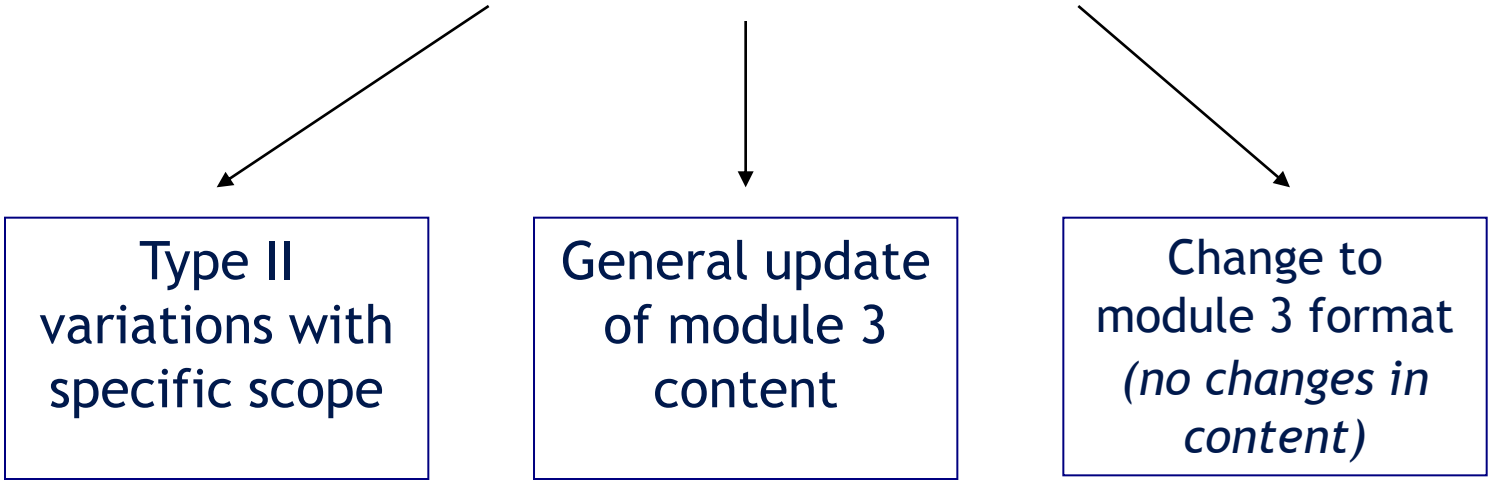
(a). MRP-like procedure national variations to module 3

- National type II variations waiting for assessment
  - ✓ List of ID numbers will be published on website.
  - ✓ Request for MRP-like + additional documentation to:

    MRP_like_quality@fagg-afmps.be

I.4. Further plans (quality assessment)

(b). FAGG proposal for national variations to module 3 that do not follow MRP-like procedure



I.4. Further plans (quality assessment)

(b). FAGG proposal for national variations to module 3 that do not follow MRP-like procedure

Type II variations with specific scope	General update of module 3 content	Change to module 3 format *(no changes in content)*

- Application form should be clear on scope, proposed changes and amendments to module 3.
- Assessment focused on proposed changes.
- Questions during procedure focused on proposed changes.
- Other concerns arising from supportive documentation considered as recommendations to the applicant (not to be cleared during procedure)

I.4. Further plans (quality assessment)

(b). FAGG proposal for national variations to module 3 that do not follow MRP-like procedure

Type II variations with specific scope	**General update of module 3 content**	Change to module 3 format *(no changes in content)*

- Application form does not compare current and proposed situation.
- Full assessment of module 3.
- All questions need to be cleared during the procedure.

I.4. Further plans (quality assessment)

(b). FAGG proposal for national variations to module 3 that do not follow MRP-like procedure

Type II variations with specific scope

General update of module 3 content

Change to module 3 format *(no changes in content)*

- Application form should clearly confirm that there are no changes in the content
- No assessment.

II. Renewals

II.1. Current status

II.2. FAGG proposal action plan for national renewals

II.1. Renewals: current status

1007 parent dossiers

- ✓ 548 paper dossiers
- ✓ 459 electronic dossiers

260 dossiers waiting for Revision/Validation

II.2. Renewals: proposed action plan

General action point:

New standard procedure for dossier management

- Information on requirements content of submission (for innovators and generics)
- 6 months maximum to respond to RFI
- 2 rounds maximum for assessment (similar to MRP/DCP procedure)

II.2. Renewals: proposed action plan

Action points for innovators:

- Worksharing with Netherlands and France: test phase ongoing
- Core Safety Profile as agreed in PSUR Worksharing
- Not marketed Medicinal Product: risk analysis

Action points for generics and copies:

- Marketed medicinal products: Alignment on innovator
- Not Marketed medicinal products: risk analysis

II.2. Renewals: proposed action plan

Actions for Renewals waiting for Revision/Validation :

- Management of the dossier after consultation of the responsible of the experts
- First phase :Validated leaflets
- Second phase: Non validated leaflets

Thank you

Federal Agency for Medicines and Health Products
(FAMHP)

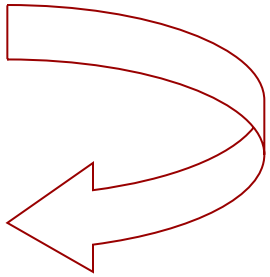
Autocontrole

Wim Penninckx
Evaluators, *division head a.i.*

11.12.2009

Conditions

- Control procedures implemented at company level.
- Sampling and testing by FAMHP.
- Sanctions where necessary.



Legal basis to be created

Autocontrole implemented in …

- Declaration of conformity translations SPC, leaflet and labelling.
- System for “Readability testing”.
- System for Type I variations.
- MRP-like procedure for analytical type II variations.
- …

Autocontrole foreseen for …

- Compliance with QRD template at time of renewal
- Type II variation consequential to PSUR assessment
- “ Recommendations” made during assessment analytical type II variation.
- …

Questions and answers

Pause-café

Koffiepauze

Programme: deuxième partie

- **Implémentation nationale du nouveau variations Regulation (EC/1234/2008) (AFMPS)**

  Présentations (35 min)

  Législation et procédures (Iris Geussens)

  Adaptations MeSeA et Mails automatiques (Ann Verhoye)

  Questions and answers (30 min)

Federal **A**gency for **M**edicines and **H**ealth **P**roducts
(FAMHP)

BETTER REGULATION
GROUPED VARIATIONS IN MESEA & AUTOMATIC MAILS

Ann Verhoye
Iris Geussens

Brussels, 11 december 2009

Grouped variations in MeSeA

Submission of grouped variations: one or several CTD tree structures in NeeS or eCTD format per MP or per MA

MeSeA:

1 upload

1 workflow

1 automatic mail for the whole group

Dossier subject provides details on MP names and concerned variation subjects

Partial negative advice/ withdrawals treated Separately at end of assessment phase/on ad hoc basis

Grouped variations in MeSeA

! Attention points before submission:

1. Provide all **details** regarding the concerned medicinal products and variation subjects in the **AF** since dossier subject mentioned on automatic mail will be based on AF.
2. Keep in mind that highest ranking variation within the group determines the timetable of all variations included in the group!
3. NEW: entry date will be mentioned within dossier characteristics: entry date before 01.01.2010: current implementation rules
4. Implementation of type II variations is based on Round Up mail, this means that this triggers the deadline for publication of updated PIL/SPC! → communication PUM
5. Decimal fees and new indexation in force for all submissions received starting from 01/01/2010!

Automatic mails – acknowledgement of receipt

NAT type IA :

stop implementation **immediately** if FAMHP comments received within detailed response time

'**NAT type IB** (stand alone or highest ranking):

start implementation period upon reception of approval FAMHP or in case of absence of comments FAMHP 30 days after validation

NAT type IB (part of group but not highest ranking):

start implementation period upon reception of Round Up mail (highest ranking: type II or line-extension).

Automatic mails – acknowledgement of receipt

MRP CMS type IA :

stop implementation immediately if RMS refuses the notification.

MRP CMS type IB :

start implementation period upon reception of approval RMS or in case of absence of comments RMS 30 days after validation

MRP CMS type II:

Implementation possible 30 days after approval of RMS, on condition all necessary documents submitted within those 30 days – use **exact** translation of European documents for the national implementation

Automatic mails – acknowledgement of receipt

Wait for **additional** AMM before implementation!

Response times mentioned in automatic mail include validation period and timetable period.

Type IB variation:

validation period: 7 days + 7 days (unforeseen type IB variation)

Type II variation:

validation period: 14 days

Art 5 of Commission regulation EC/2008/1234 in case of default type IB submission without copy of CMDh advice.

Automatic mails – dossier receipt not OK

Only in case of dossier rejection.

Warning that administrative fee needs to be paid: 279 euro (new index: 276,14)

Automatic mails – payment tracking

Payment tracking OK

In case there is sufficient provision.

Payment tracking not OK

In case there is insufficient provision.
For details contact fin@fagg-afmps.be .

Automatic mails – start assessment

MRP RMS type IA :
stop implementation immediately if RMS refuses the notification.

MRP RMS type IB (stand alone or highest ranking):
start implementation period upon reception of approval FAMHP or in case of absence of comments FAMHP 30 days after validation

MRP RMS type IB (part of group but not highest ranking):
start implementation period upon reception of NoA of FAMHP (highest ranking: type II or line-extension).

Automatic mails - Round Up

NAT type II (both analytical and clinical – stand alone or highest ranking):
Start implementation period 30 days after reception of Round Up mail

Condition: closing documents submitted to FAGG closing mailbox within 30 days.

Implementation can be initiated based on automatic mail without updated AMM, except in case and ADDITIONAL AMM is needed.

NAT line-extension: wait for AMM for implementation

Automatic mails – Effect Changes

Notification that internal data base will be updated and that AMM and annexes will be send soon

Automatic mails - Example

Type IA variation – national procedure in group with type II variation – national procedure:

Entry date: 04/01/2009

Stop implementation: 19/03/2009 (= 74 days later in case of 60 day type II TT and no clock-stop)

Type IB variation – national procedure in group with type II variation – national procedure:

Entry date: 05/01/2009

Start implementation: date of round up mail (theoretically: 20/03/2009 = 74 days if no clock stop and 60 days TT)

Implementation done: date round up mail + 6 months (theoretically: 20/09/2009)

Automatic mails – Example

Type II variation – national procedure in group with type IB variation – national procedure:

Entry date: 04/01/2009

Start implementation: date of round up mail + 30 days on condition that national closing documents were submitted

(theoretically: 18/04/2009 = 74 +30 days)

Implementation done: 6 months after start implementation (theoretically: 18/10/2009)

Type IB variation – MRP RMS procedure in group with line-extension – MRP RMS procedure:

Entry date: 05/01/2009

Start implementation: 19/04/2009 (= 104 days = line-extension approval date if no clock stop)

Implementation done: 19/10/2009

Automatic mails - Example

Type IA variation – MRP RMS procedure in group with type IB variation – MRP RMS procedure:

Entry date: 04/01/2009

Stop implementation: 17/02/2009 (44 days later = type IB approval date if no comments)

Type II variation – MRP RMS procedure in group with type IA – MRP RMS procedure:

Entry date: 06/01/2009

Start implementation: 21/03/2009 (= 74 days later = type II approval date in case of 60 day TT and no clock stops)

Implementation done: 21/09/2009

Automatic mails - Overview mails

Variation IA/IB – NP or MRP CMS and Variation type II analytical – MRP CMS:

Acknowledgement of receipt mail

Payment mail

Variation IA/IB/II – MRP RMS – variation type II clinical MRP CMS – variation type II NP

Acknowledgement of receipt mail

Payment mail

Start assessment mail

Round Up mail

Before effect changes mail

Better Regulation - questions & answers

Do and tell:

Examples of immediate notification type IA

→ Change in name and/or address of MAH

→ Tightening of specification limits for medicinal product subject to official batch release

→ Changes in imprints, bossing or other markings of finished product

→ Change of pack sizes within the range

→ Change in SPC, PIL, labelling due to referral (art.34 and 38) for medicinal product covered by defined scope of referral

→ see also Commission Classification Guideline:

http://ec.europa.eu/enterprise/pharmaceuticals/varreg/pubcons_2009-07.htm

Better Regulation - questions & answers

Do and tell

Immediately stop implementation of IA after refusal

• Definition of "immediately":
→ if European consensus exist: will be followed by FAMHP

• Impact on the market
→ Minor variations: low risk for public health
→ raison for refusal:
not paid,
not complete
→ responsibility of applicant

Better Regulation - questions & answers

Implementation of Type II variations:

→ not before: approval date + 30 days if documents are submitted

→ no later then: approval date + 30 days + 6 months

Better Regulation - questions & answers

Implementation of Type II variations:

- How to submit?

  → By mail to FAGG_closing_file@fagg.be

- When to submit?

  → As soon as possible and within 30 days after approval.

- How ?

  → exact translation of final SPC, PIL and labelling

  → no national interpretation of the final documents

  → if no harmonized PIL and labelling: wait until approved MA

Better Regulation - questions & answers

Implementation of Type II variations:

• What in case of comments on PIL and labelling already released for market?

→ adaptation of SPC, PIL and labelling to comments
→ implemented within 6 months from date on MA.
→ impact on market: depending on risk public health

Better Regulation – questions & answers

Implementation of Type II variations:

• What in case of comments on PIL and labelling already released for market?

Reminder: points of attention for closing:

- name + strength + pharmaceutical form
- QRD-template
- standard terms for pharmaceutical form, method of administration, storage conditions

Better Regulation - questions & answers

Implementation of Type II variations:

• What in case of comments on PIL and labelling already released for market?

Reminder: **points of attention for closing**:

- conformity between SPC, PIL, Labelling, Mock-up and MA.
- declaration of conformity
- blue box requirements

! Not only for new medicinal products but also for already existing medicinal products !

Better Regulation - questions & answers

Adaptation of the MA:

- Better Regulation:
  - → type IA: annual reporting: 2 months
  - → type IA_{in} : 6 months
  - → type IB: 6 months
  - → type II: 2 months

- FAMPS: as good as possible
  - → help needed from applicant:
    - good quality of closing documents
    - good time management

Better Regulation - questions & answers

Grouping:

- Procedure: ex. group of 1 type II, 2 type IB and 1 type IA

→ consequential or linked (annex III of Regulation):
unavoidable + direct result of change
not simply at the same time

→ one dossier: one cover letter, one application form, one form for payment

→ fees: same rules, but with decimal

→ procedure nr: ex. BE/H/415/II/035/G

Better Regulation – questions & answers

Grouping:

- Procedure: ex. group of 1 type II, 2 type IB and 1 type IA

→ decision for each variation

→ implementation:

II: approval date + 30 days

IB: from approval date

IA: already implemented

Better Regulation – questions & answers

Grouping:

Acceptable:

1. type II (III.1_6a) for new indication + type IB/IA (II.2.e_5a) addition of new pack size corresponding to new indication.

2. Extension for new strength/pharmaceutical form + type II (III.1_6a) for new indication used with this new strength/pharm. Form.

3. Type II (III1_6a) new indication + Type II (III.1_5b) switch to OTC.

4. Type II (III.1_4) update safety information section 4.8 + Type II (III.1_4) update section 4.9 with overdose information

Better Regulation - questions & answers

Grouping:

Not Acceptable:

1. data package supportive of 2 different indications e.g. renal cell carcinoma + non-small cell lung cancer

2. Update safety information in section 4.8 + update section 5.2 with PK data.

3. Update safety information in section 4.4 and 4.8 + update section 4.5 with new interaction study results + update section 5.3 with results of toxicity study in juvenile rats

Important Communications

Holidays:

FAMPS closed between 24/12/09 and 4/1/2010.

Transition period:

→ due to Better Regulation and adaptation of MeSeA

→ Recommendation not to introduce variations between 15/12 and 31/12/09.

Inactivation:

→ Applicable time suspended during Holidays.

→ Starts again form 4/1/2010

Important Communications

New important e-mail addresses:

changecontact@afmps.be:

for changes in general e-mail address.

Aflevering_delivrance@fagg-afmps.be:

correction of reference of delivery modus on MA.

radiation@fagg-afmps.be:

for radiation of MA asked by the MAH.

Important Communications

Other important e-mail addresses:

dispatching@fagg-afmps.be:

to submit registration dossiers.

Gestion.fagg-afmps@fagg-afmps.be:

to submit answers on questions raised during procedure.

VARANA@fagg-afmps.be:

to submit answers on questions raised during the procedure for NP IB variations

Important Communications

Other important e-mail addresses:

Fagg_closing_file@fagg-afmps.be:

to submit closing documents.

registration@fagg-afmps.be:

call center: questions on status of the dossier, corrections of documents, inactivation, withdrawal letter Backlog, priority, …

uniqueregistrationnumber@fagg-afmps.be:

to ask unique registrationnumber if a dossier is submitted

Better Regulation - Automatic mails

Thank you for

Your attention !!!

Questions and answers

Clôture

Virginie Peirs
Director Regulatory Affairs FeBelGen