Mutual recognition and Decentralised procedures

Florida University Pharmacy Students' Visit to AIFA

Sandra Petraglia
AIFA

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Interests in pharmaceutical industry	NO	Currently	Last 2 years	More than 2 years but less than 5 years ago	More than 5 years ago (optional)
Direct interests:					
Employment with a company	X				
Consultancy for a company	X				
Strategic advisory role for a company	X				
Financial interests	X				
Ownership of a patent	X				
Indirect interests:					
Principal investigator	X				
Investigator	X				
Individual's Institution/Organisation receives a grant or other funding	X				

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“European” procedures

- Multistate Procedures

- Mutual Recognition Procedure
- Decentralised Procedure

MRP/DCP

- Eligible for all active substances outside of the mandatory scope for centralised procedures (including herbals and homeopatics, if according to the provisions of artt. 16.1 and 16d of Directive 2001/83 as amended)
- Eligible for all legal basis

MRP/DCP

- Eligible for initial applications and additional strenght/form (line extension)
- Both eligible for inclusion of additional MSs (repeat use) in subsequent waves
- Both allowed to be run for additional identical dossier in parallel procedures (multiple or duplicate applications)
- Dossiers authorised by MRP/DCP remain harmonised throughout their whole lifecycle

MRP/DCP

- Same legal requirements and dossier structure as nationally autorised and centralised procedures
- Administrative validation at European level, in the respect of national requirements
- Scientific assessment at European level
- Final agreement on acceptability at European level
- Marketing authorisation: national

MRP and DCP

Two routes to receive a MA

1. Mutual recognition procedure (MRP)

   where the medicinal product has already received in a MS a Marketing Authorisation at the time of application

or

2. Decentralised procedure (DCP)

   where the medicinal product has not received in a MS a Marketing Authorisation at the time of application

Mutual recognition procedure

- Medicinal product already authorised in 1 Member State
- Identical dossier
- Initial MS: Reference MS
- Additional MS(s): Concerned MS(s)

Mutual recognition procedure

- RMS prepares/updates Assessment Report
- AR is sent to the list of CMS(s) together with SmPC, PL, labelling
- Approval within 90 days
- National Marketing Authorisation in CMS(s) within 30 days

MRP: flow chart

- Day 90: end of procedure – start of the national phase in the CMSs (check translation of product information and granting of a marketing authorisation within 30 days)

or

- Day 90: end of procedure with potentially serious risks for public health unsolved and consequent referral to CMDh

Decentralised Procedure- flow chart

- Medicinal product not yet authorised in any MS at the time of application
- Identical dossier
- Choice of RMS by the applicant
- Additional MS(s): Concerned MS(s)

Decentralised Procedure

- The reference Member State shall prepare a draft assessment report within 120 days after receipt of a valid application

- Within 90 days of receipt of the draft assessment report the MS shall either approve or reject the procedure: same as MRP.

Decentralised Procedure

Step I

- RMS: pre-submission meeting
- Validation phase (day -14/day0) in parallel in both RMS and CMS
- RMS: sends PrAR to all CMS at day 70
- CMS(s): send comments to RMS by day 100
- Day 100-105: consultation among RMS, CMS and applicant
- Day 105: RMS prepares the LoQ for the applicant
- Clock stop: the Applicant prepares the response document – RMS drafts the DAR

Decentralised Procedure – flow chart

Step II

- RMS: at day 120 sends the DAR to the CMS(s)
- CMS(s) : send comments by day 145
- RMS: receives the applicant's responses at day 160 and sends a short report to CMS(s) by day 180
- RMS and CMS: possibility of a Break Out Session at the EMA around day 205
- CMS: final comments at day 195

Decentralised Procedure – flow chart

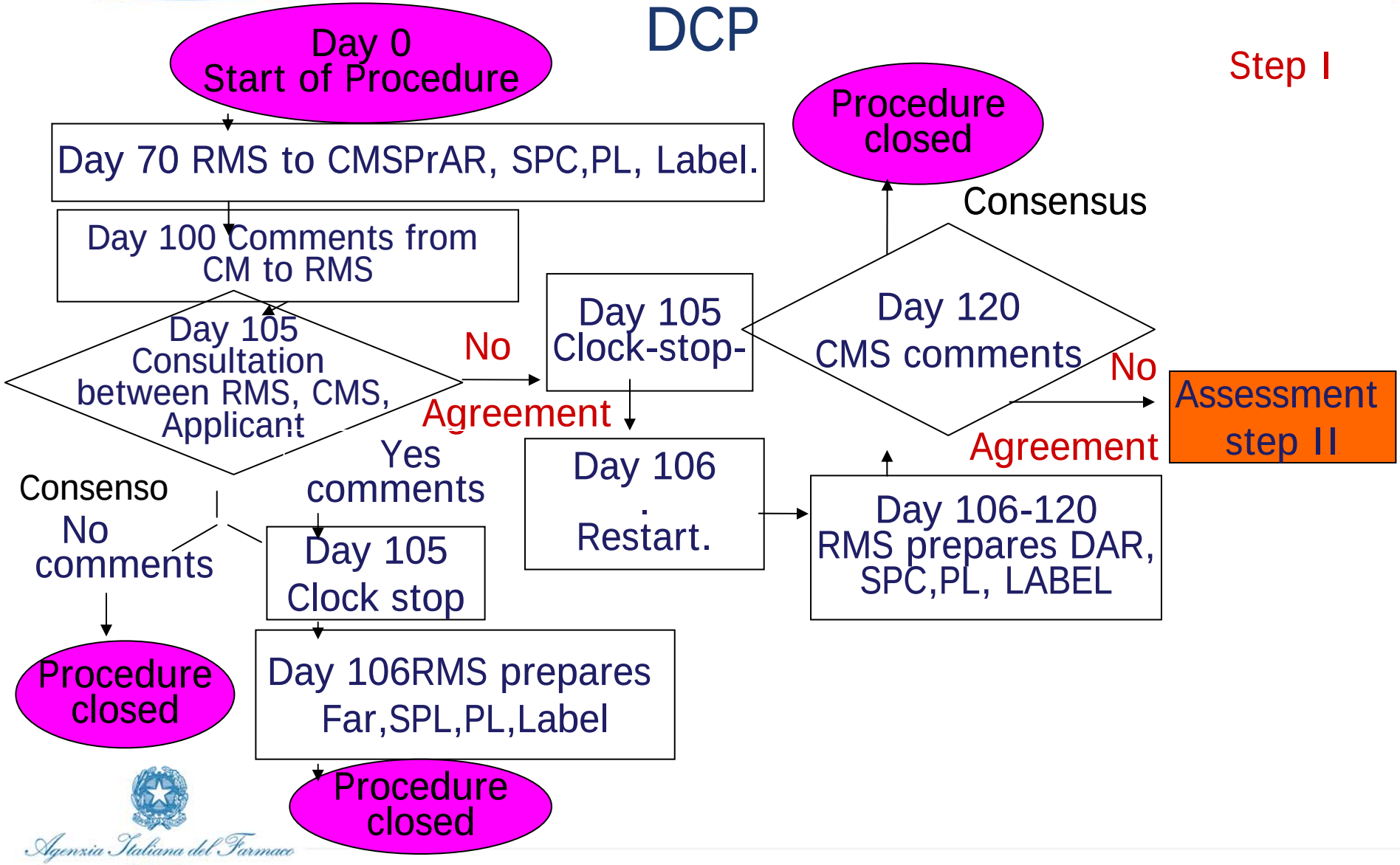
- Day 210: end of procedure – start of the national phase in RMS and CMSs (check translation of product information and granting of a marketing authorisation within 30 days)

or

- Day 210: end of procedure with potentially serious risks for public health unsolved and either refusal of the DCP (if RMS) or referral to CMDh (if CMS)

DCP

Step I



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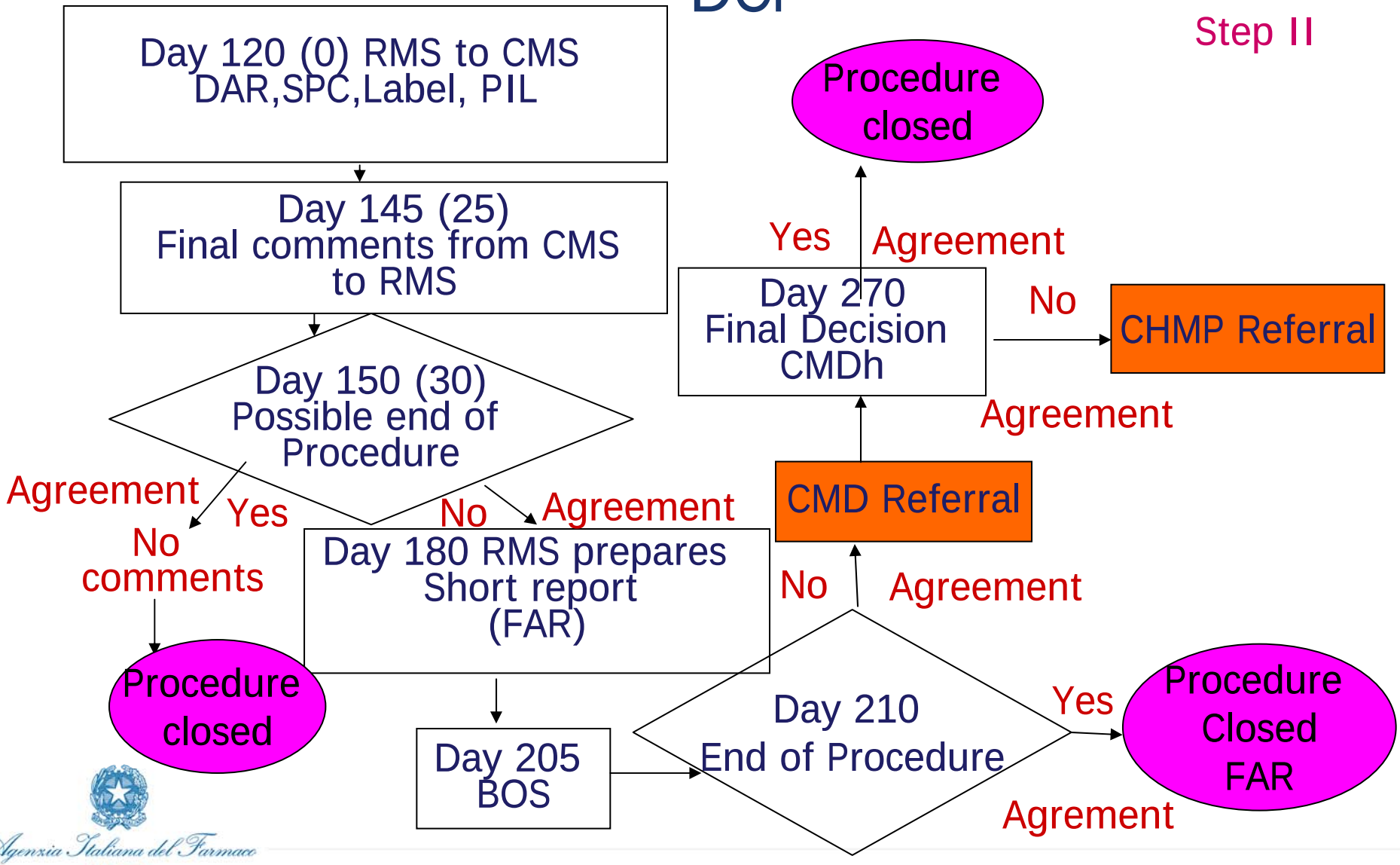
DCP

Step II



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The DCP – superior model or simply a twin of MRP?

Similarities:

- 90 days phase
- Possibility to submit in 1 to 30 MS
- Both procedures can be used for line extensions of a previous marketing authorisation
- Possibility to have a different trademark in different MS
- Same standard of evaluation
- Same final national phase (30 days)

The DCP – superior model or simply a twin of MRP?

Differences - MRP:

- Medicinal product already authorised
- Need for a preliminary national approval/update
- RMS has to “support” the dossier
- SmPC already approved
- One phase only for assessment
- No possibility to avoid a referral
- The content of the dossier is fixed and there is no possibility to update it without further prolonging the national phase

The DCP – superior model or simply a twin of MRP?

Differences - DCP:

- New medicinal product
- RMS assesses the dossier for the first time, “in parallel” with CMSs – dossier updated at the start
- SmPC not yet approved
- Two phases for assessment
- The content of the dossier can be updated during the clock-stop (user testing, GCP, GMP, new studies, other data?)

The DCP – superior model or simply a twin of MRP?

Differences - DCP:

- No referral for withdrawals before day 120 (commercial reasons only)

- Possibility of an earlier closure any time after day 120

- Possibility of a negative opinion from the RMS

MRP/DCP validation phase

- Cover letter and application form + Module 1
- Check of legal basis and administrative details, including fees
- Possibility of additional national requirements for each MS, on the basis of national legislation

MRP validation phase

Synthon ruling by the ECJ (*November 2008*)

- Decision on validation by the RMS to be followed by the CMS(s) – including legal basis
- Conclusions of the RMS as reported in the Assessment Report to be accepted by the CMSs, unless potential serious risks to public health in accordance with the Commission Guideline are highlighted

- *The possibility to comment on MRP and influence its outcome by the CMS(s) has been strongly limited by this sentence*

MRP/DCP national phase

Positive outcome:

- Check of national translations of SmPC, PL and labelling
- Check of administrative details and manufacturing sites
- Drafting of the MA (legally binding document)
- RMS: drafts and publishes the Public Assessment Report on the MR-Product Index (and on the national website)
- All MS: publish SmPC and PL on their national websites

MRP/DCP national phase

Negative outcome:

1. Potentially serious risks to public health raised by a CMS: referral to Coordination Group (both MRP and DCP) and start of the 60 days referral phase

2. Potentially serious risks to public health raised by RMS: refusal of the procedure in all MS (no possibility of appeal)

CMDh referral

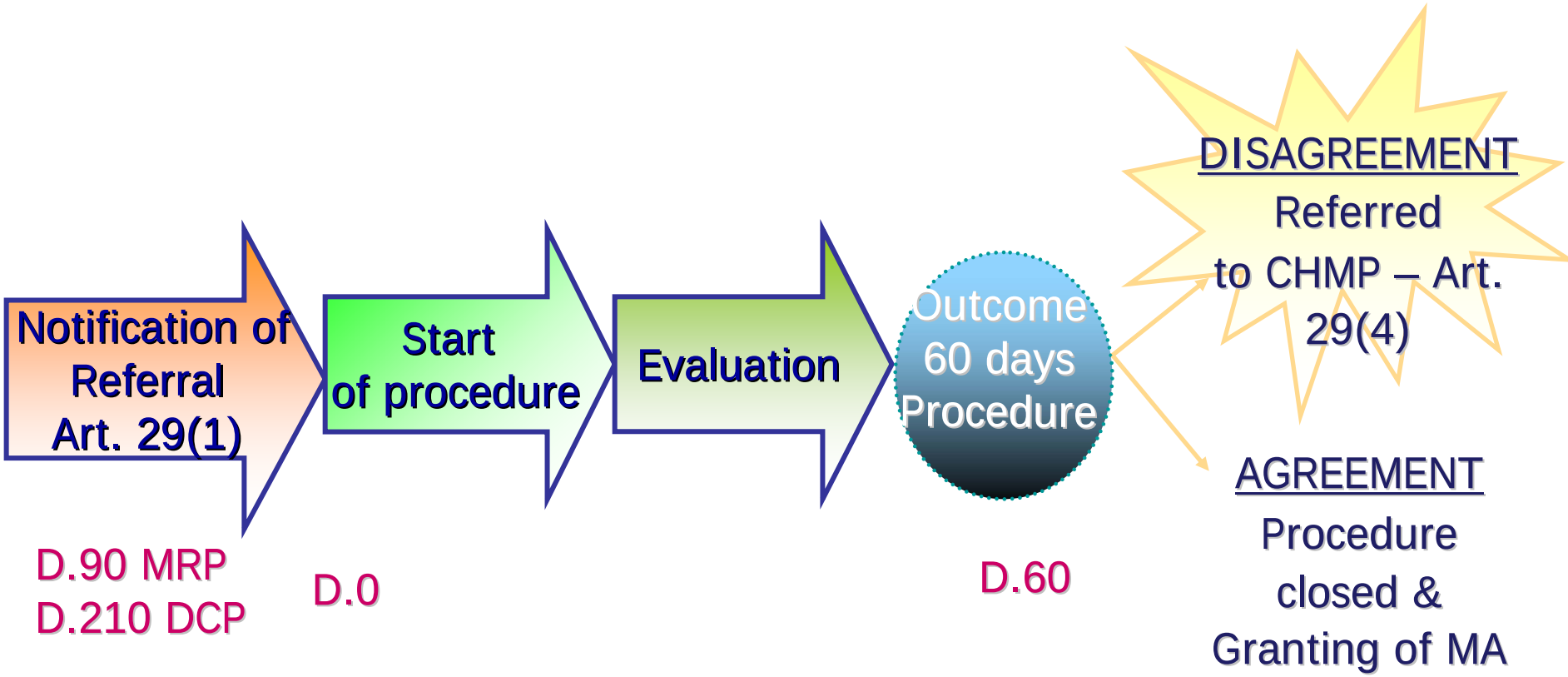
Trigger:

Disagreement between MS concerned by the application at the end of MRP (Day 90), DCP (Day 210), type II variation or Worksharing procedure based on potential serious risk to public health.

The withdrawal of the Application in the disagreeing MS no longer prevents a referral to the CMD(h) and CHMP

CMD(h) is not empowered to reject a Referral if a MS concerned by the procedure claims a potential serious risk to public health related to the approval of an application for a marketing authorisation.

CMD(h) & The 60-day Procedure



CMD(h) & The 60-day Procedure

Outcome of discussions

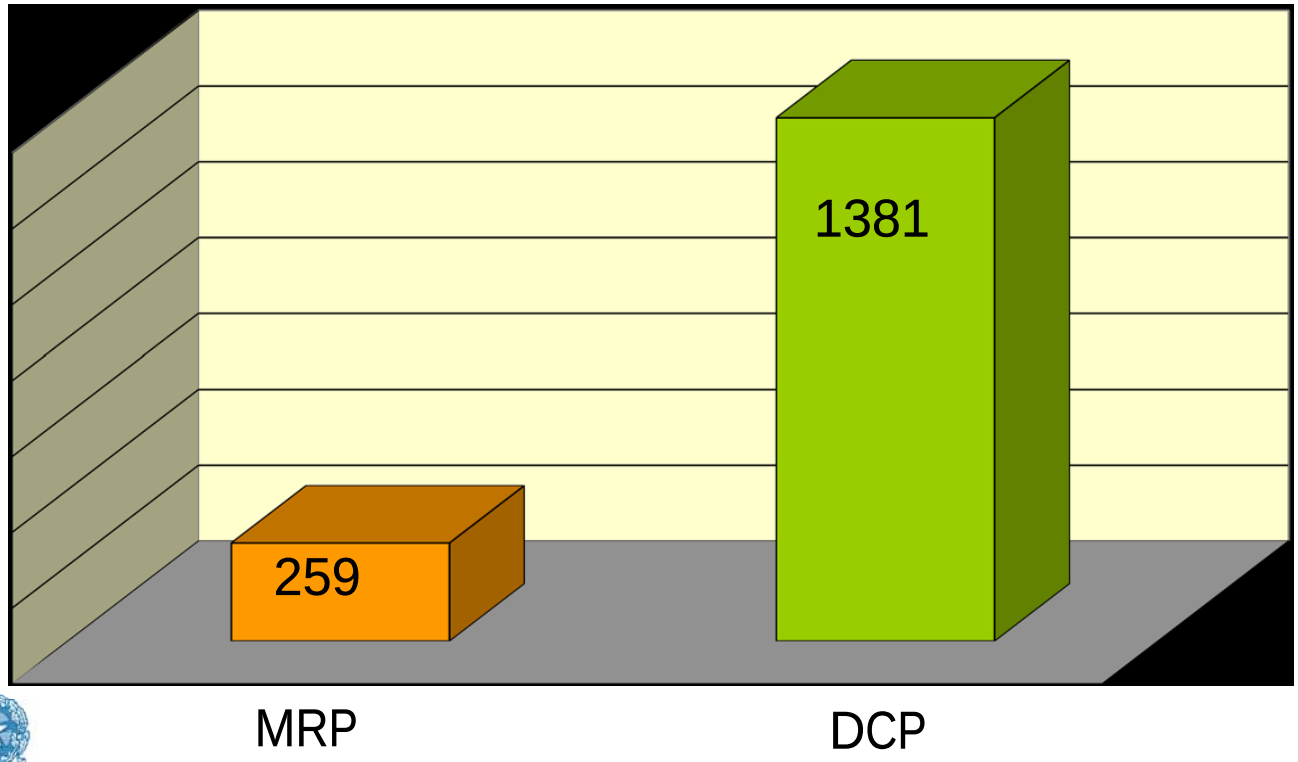
☑ Agreement reached: The RMS shall record the agreement, close the procedure and inform the applicant accordingly. National phase starts.

☒ Agreement not reached: the Agency shall be immediately informed, with a view to the application of the procedure under Articles 32, 33 and 34 of Directive 2001/83 and shall be provided with a detailed statement of the matters on which the MS have been unable to reach agreement and the reasons for the disagreement. CHMP referral starts.

MRP/DCP statistics – new applications 2011

FINALISED Procedures

Total: 259 MRP and 1381 DCP (regarding 515 and 2934 products respectively)



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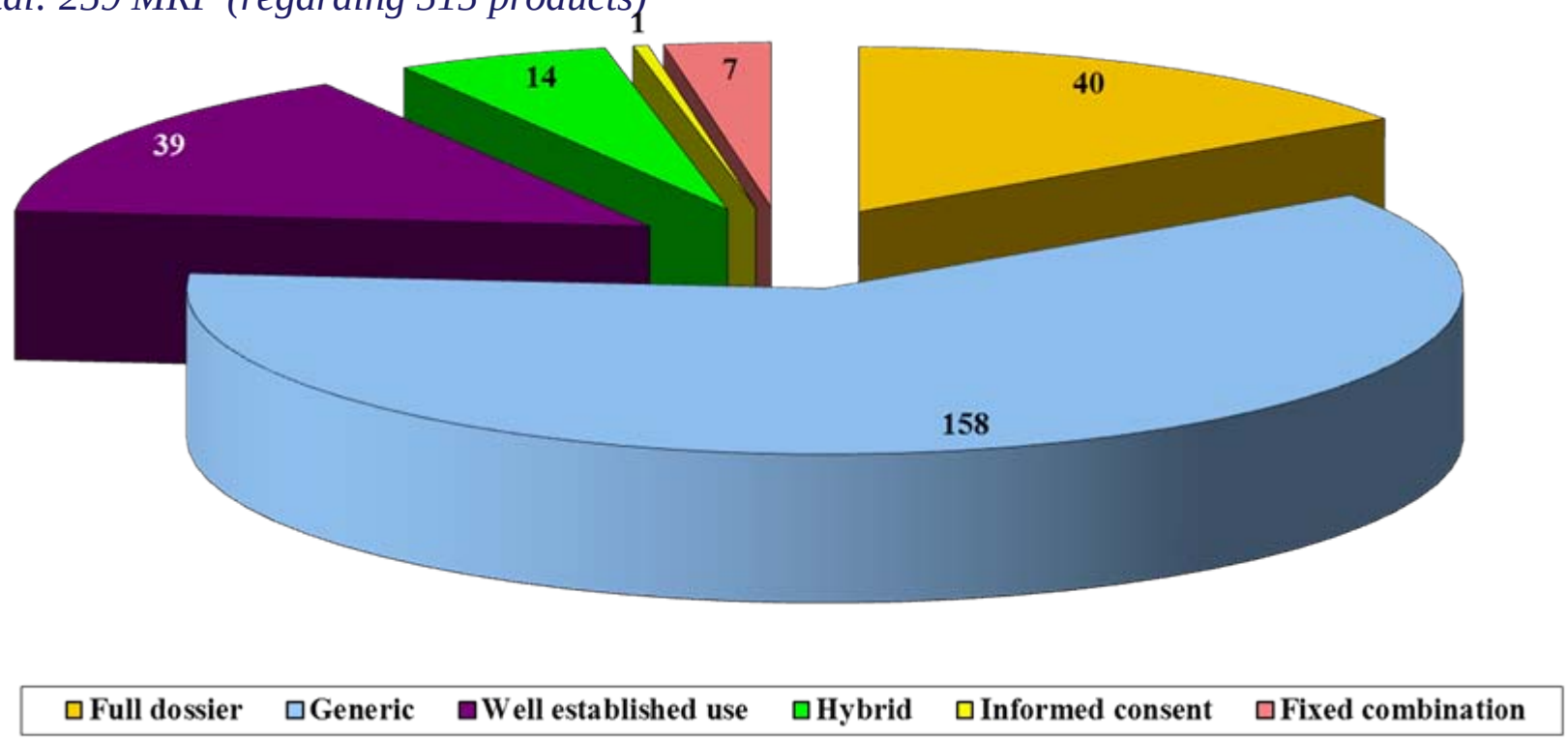
MRP/DCP New applications - 2011

FINALISED Procedures - MRP per legal basis

Total: 259 MRP (regarding 515 products)



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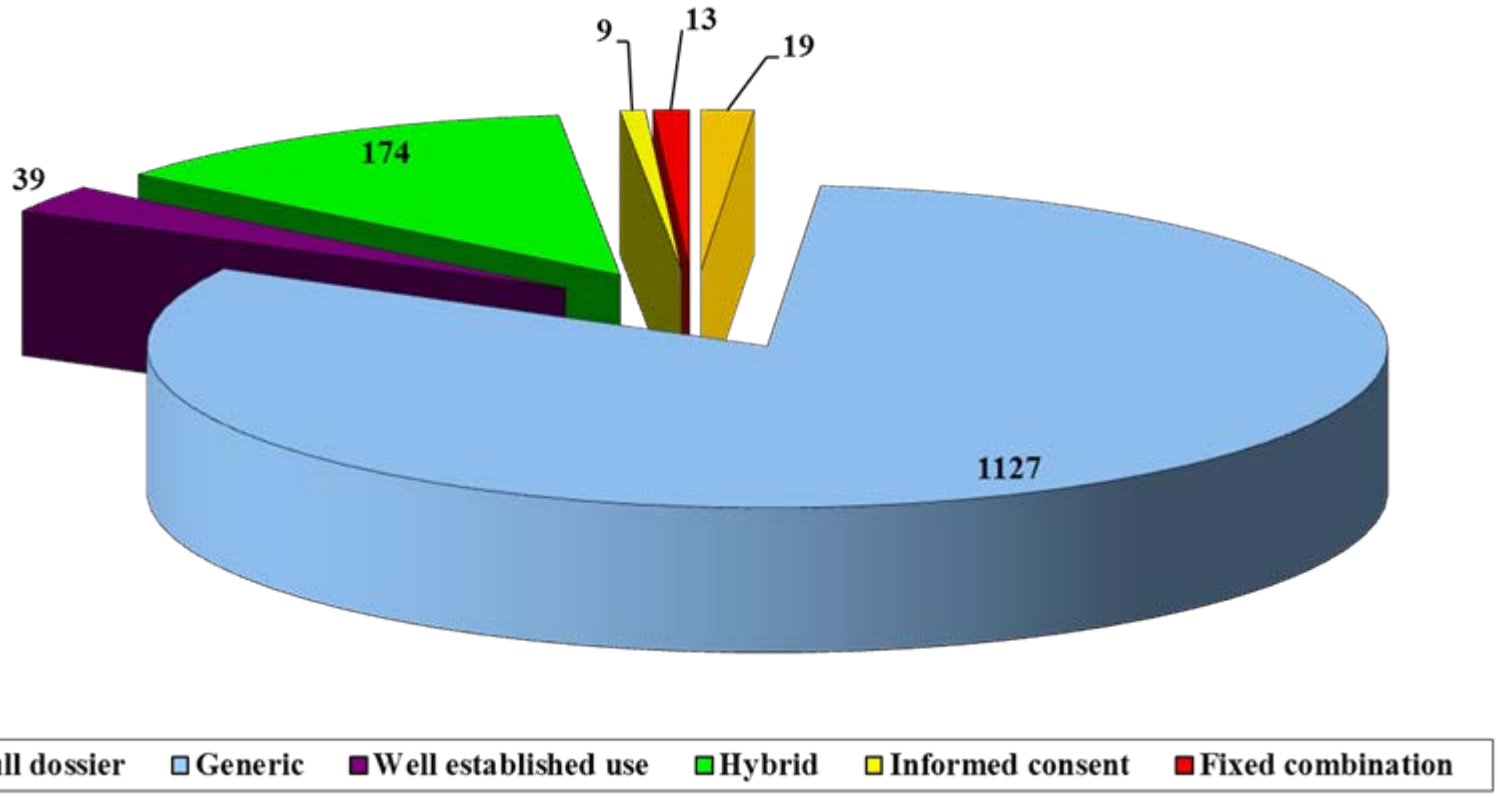
MRP/DCP New applications - 2011

FINALISED Procedures - DCP per legal basis

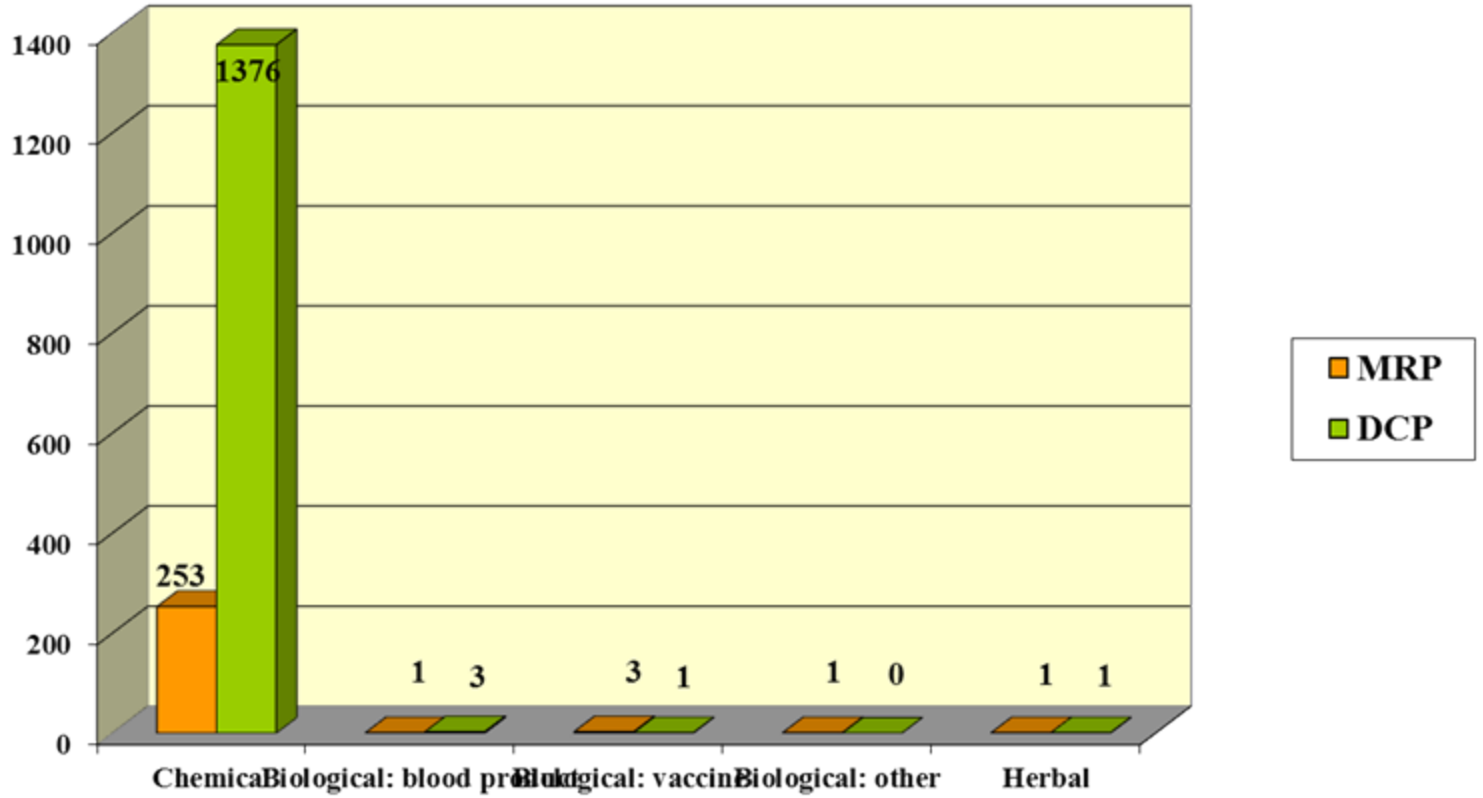
Total: 1381 DCP (regarding 2934 products)



MRP/DCP New applications - 2011

FINALISED Procedures – MRP/DCP per type of product*

Total: 259 MRP and 1381 DCP (regarding 515 and 2934 products respectively)



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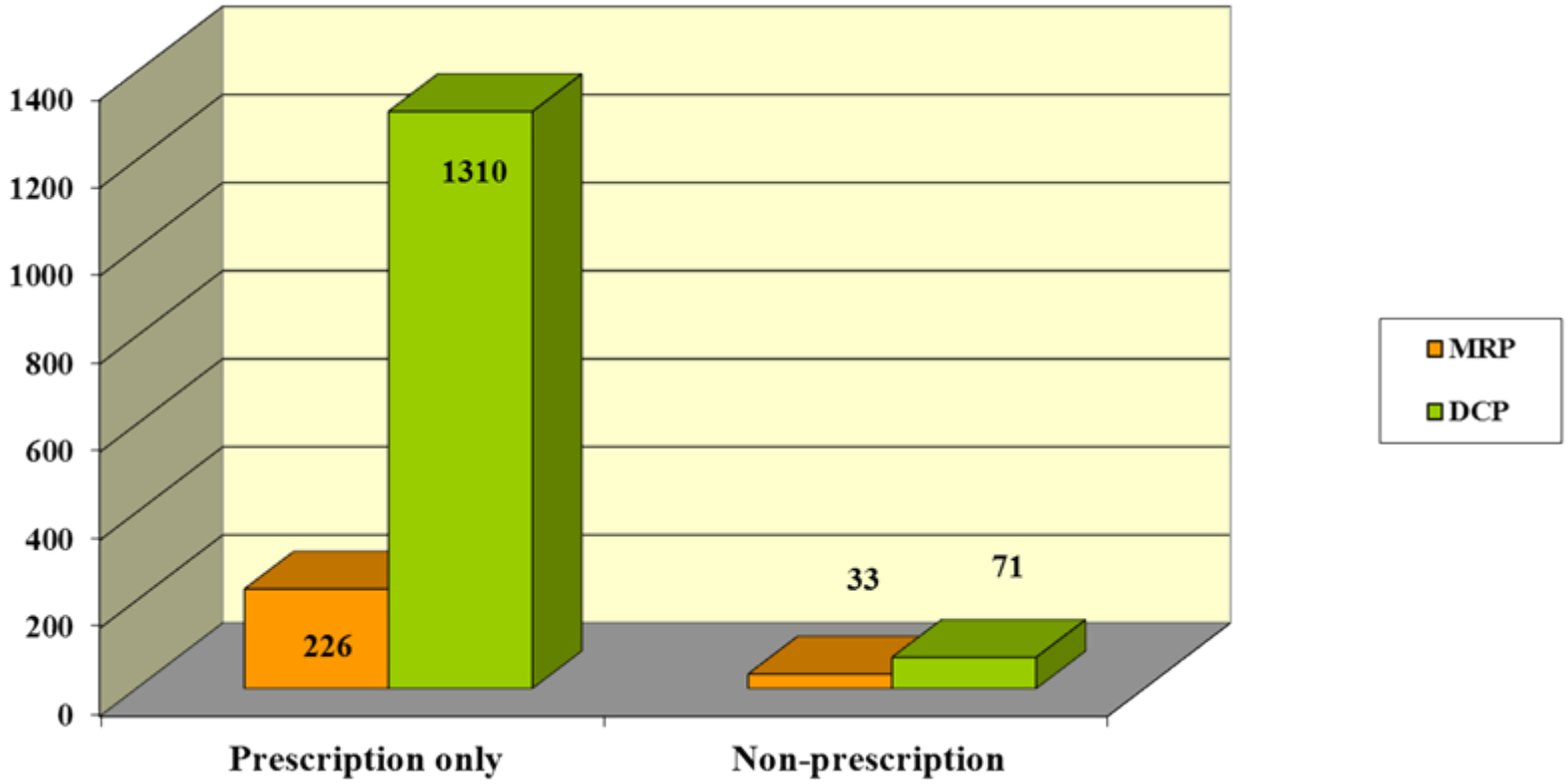
MRP/DCP New applications - 2011

FINALISED Procedures – MRP/DCP per prescription status *(as approved by the RMS)*

Total: 259 MRP and 1381 DCP (regarding 515 and 2934 products respectively)



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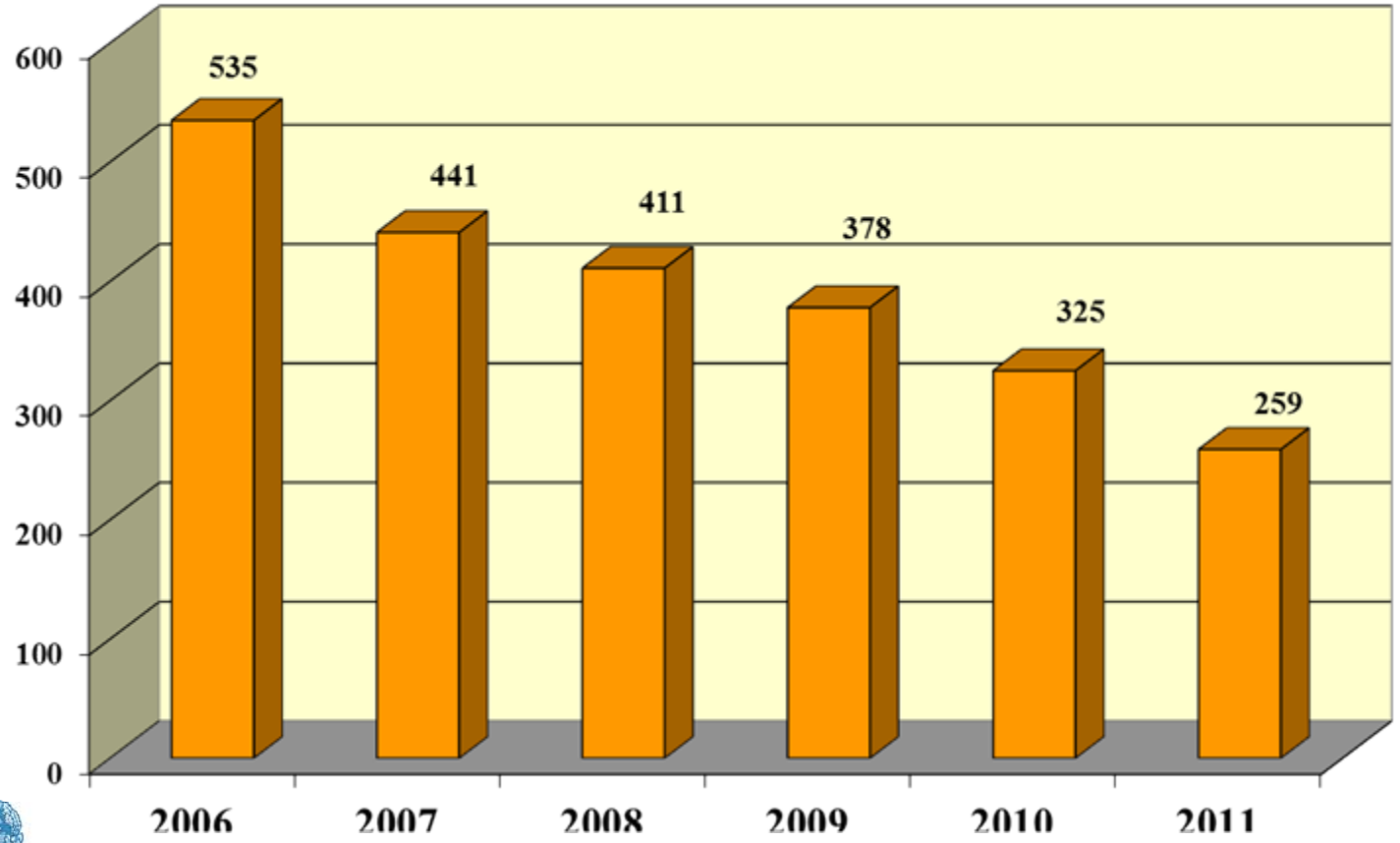
MRP/DCP New applications 2006-2011

FINALISED Procedures – MRP



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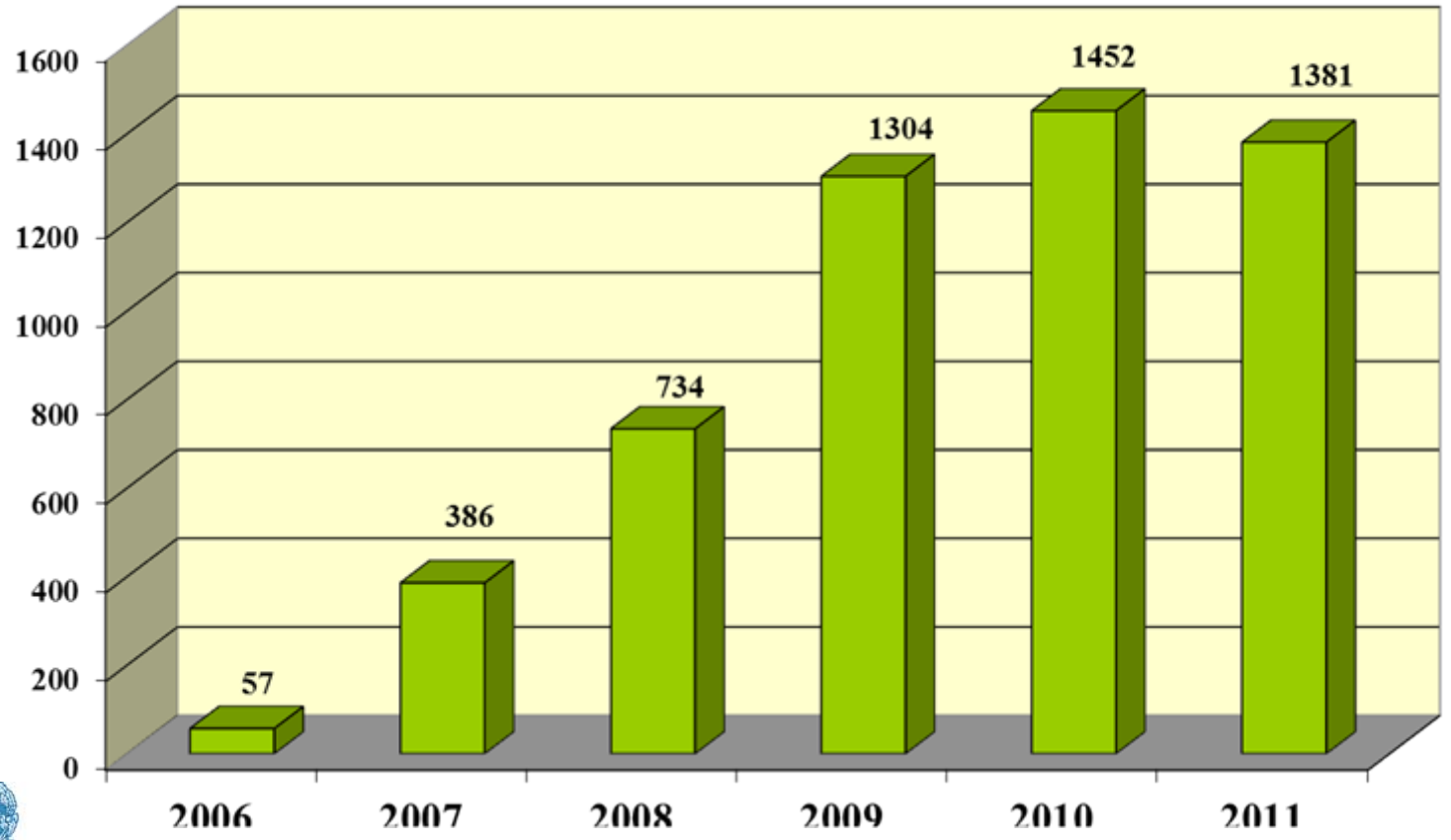
MRP/DCP New applications 2006-2011

FINALISED Procedures –DCP



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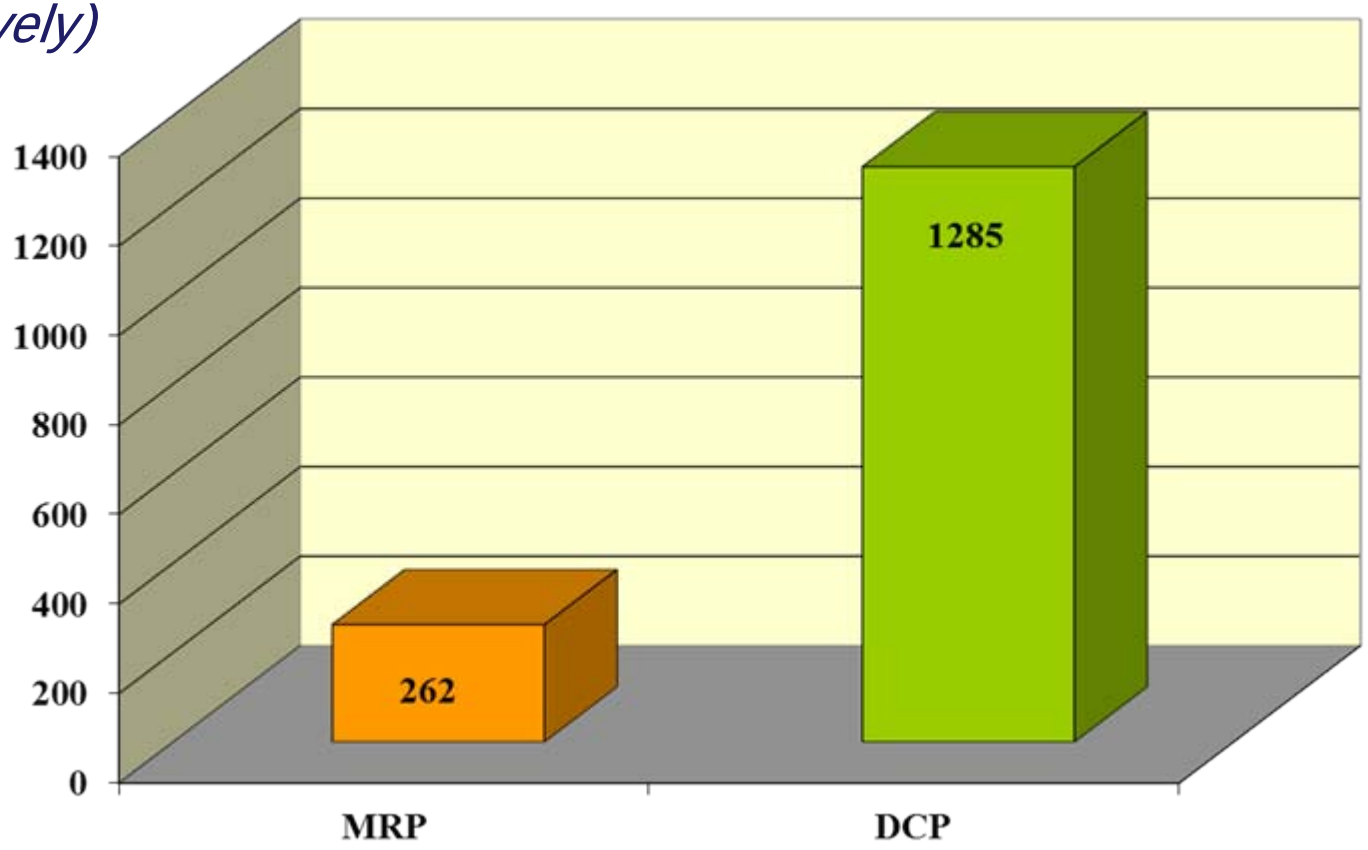
MRP/DCP New applications - 2011

STARTED Procedures

Total: 262 MRP and 1285 DCP (regarding 521 and 2549 products respectively)



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Legislation and guidance

- Directive 2001/83 and amendments
  http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2001L0083:20110721:EN:PDF

- EC Guideline on the definition of potential serious risk to public health
  http://ec.europa.eu/health/files/eudralex/vol-1/com_2006_133/com_2006_133_en.pdf

- Notice to applicants (vol. 2)
  http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm

- BPG/SOP, Q&A and specific guidance: CMDh website
  http://www.hma.eu/cmdh.html

CONTATTI

E s.petraglia@aifa.gov.it

www.agenziafarmaco.gov.it

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