

European approach to OINDP

Diana A. van Riet – Nales, 8 November 2006

IPAC-RS, Washington DC

**RIVM working for Dutch competent
authority, the MEB (NL)**

Presentation overview

- EU regulatory framework
- history of OINDP guidance
- EU regional requirements HC-EU guideline
- future harmonisation

rivm

IPAC-RS Conference November 2006
2

European Union



number of inhabitants (million)
EU 450, US = 281



current members
acceding countries
candidate countries
potential candidate countries
application frozen
application rejected by EC
accession rejected in a referendum

rivm

EU regulatory framework

European Union

- created on 1 November 1993 when Treaty came into effect
- followed several predecessors
 - European Coal and Steel Community (1952)
 - European Economic Community (1958)
 - European Community (1967, merger of ECSC, EEC and European Atomic Energy Community)
- currently 25 member states
 - + BUL + ROM from 1-1-2007
 - + IC + NO for medicines

rivm

EU regulatory framework

IPAC-RS Conference November 2006

4

European regulatory framework

- 4 application procedures
 - national procedure
 - Mutual Recognition Procedure
 - Decentralised Procedure
 - Centralised Procedure (EMA)
- assessments based on EU directives and regulations, further detailed in guidelines
- CMC guidelines developed by EMAs QWP

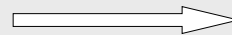
riym

IPAC-RS Conference November 2006
5

EU regulatory framework

In conclusion

- EU member states acknowledge need for harmonisation over a long period of time: many countries are simply too small to do everything by themselves
- EU has a long history of harmonisation
- EU is positive to new partnership



riym

IPAC-RS Conference November 2006
6

EU regulatory framework



Collaboration EU + HC is logical when it turns out

- EU shares most of HC proposals for regulation of OINDP
- existing EU GLs are outdated
- OINDP often globally marketed, meaning industry will profit from harmonised guidance

rivm

IPAC-RS Conference November 2006
7

History of OINDP guidance

- HC-EU GL replaces in EU
 - NfG on dry powder inhalers (1988)
 - NfG on Pressurized Metered Dose Inhalers (2002)
- GL should be consulted together with
 - PtC on Requirements for Clinical Documentation for Orally Inhaled Products (2004)
 - ICH GLs
 - CPMP GLs (www.emea.europa.eu)
 - NtA GLs (ec.europa.eu/enterprise/pharmaceuticals/eudralex)
 - Ph. Eur (www.pheur.org)

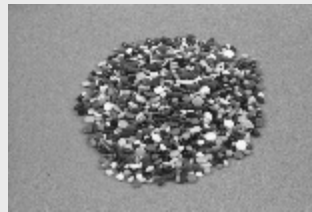
rivm

history on OINDP guidance

IPAC-RS Conference November 2006
8

Region specific aspects: generics

- therapeutic equivalence by *in-vivo* or *in-vitro* studies
 - see PtC on the requirements for clinical documentation for orally inhaled products
 - in contrast to HC, the qualitative and quantitative composition of the generic may be different from the innovator with respect to excipients
- comparability
 - always in-vitro data



rivm

EU regional requirements HC-EU guideline

IPAC-RS Conference November 2006
9

In-vitro data

- PMDI, DPI, MDN
 - complete individual stage particle size distribution profile using a multistage impactor/impinger
 - if relevant, range of flow rates
 - delivered dose



rivm

EU regional requirements HC-EU guideline

IPAC-RS Conference November 2006
10

In-vitro data

- products for nebulisation
 - complete droplet size distribution
 - output rate
 - total drug output
 - if applicable, aerosol generated with nebuliser system and settings as used in vivo



rivm

IPAC-RS Conference November 2006
11

EU regional requirements HC-EU guideline

In-vitro data

- nasal sprays
 - complete droplet size distribution
- nasal sprays and nasal powders
 - delivered dose
- nasal drops
 - droplet volume



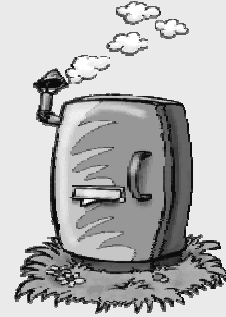
rivm

IPAC-RS Conference November 2006
12

EU regional requirements HC-EU guideline

Region specific aspects: labelling

- special focus on the use of OINDPs by patients in real life situations. Info based on development pharmaceuticals, eg:
 - shaking requirements
 - cold temperature use
 - need for priming and re-priming
 - effect of flow rate on drug performance
 - orientation of inhaler during inhalation
 - use of specific spacer/holding chamber
 - cleaning requirements



rivm

EU regional requirements HC-EU guideline

IPAC-RS Conference November 2006
13

Region specific aspects: delivery system

- fulfill requirements Annex 1 Council Directive 93/24 EEC.
- CE mark required for refillable devices
- when spacer or holding chamber is required for a specific patient population, its use should be validated
- suitability of spacers should be supported by clinical studies
- any claims on instructions for use and handling should be supported by *in vitro* data

rivm

EU regional requirements HC-EU guideline

IPAC-RS Conference November 2006
14

OINDP aspects not covered yet in a harmonised guideline

- situations where in-vitro studies can be used to waive clinical trials
 - EU reached consensus, see PtC on the requirements for clinical documentation for orally inhaled products
- acceptable limits for in-vitro equivalence
 - no EU consensus yet
 - 80-125%? per impactor stage? grouping stages acceptable?
- terminology on types of inhalers
 - change in terminology has a lot of consequences
 - currently in work programme EP expert group, however little progress

riym

future harmonisation

IPAC-RS Conference November 2006
15

Other potential areas of harmonisation relevant for OINDP

- definition of a generic
 - harmonised view allows lots of possibilities for extension of ICH topics and reduction of regional requirements in HC-EU guideline on OINDP
- role of quality assessment (not even harmonised in EU)
 - only as a means to guarantee safe and efficacious products?
 - also as a means to guarantee a consistent technical quality?
 - also as a means to guarantee good/the best available quality?

riym

future harmonisation

IPAC-RS Conference November 2006
16

Acknowledgements

Marjolein Weda, RIVM
lead expert from
the Netherlands



rivm

IPAC-RS Conference November 2006
17



rivm

Thank you for your attention

IPAC-RS Conference November 2006