The EMA Geriatric Medicines Strategy
Report from March 2012 workshop to HCP WG Meeting

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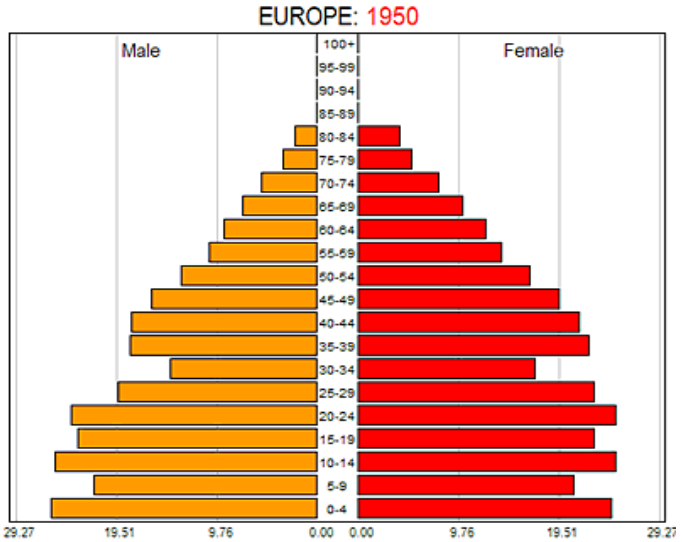
Why did we need a strategy?

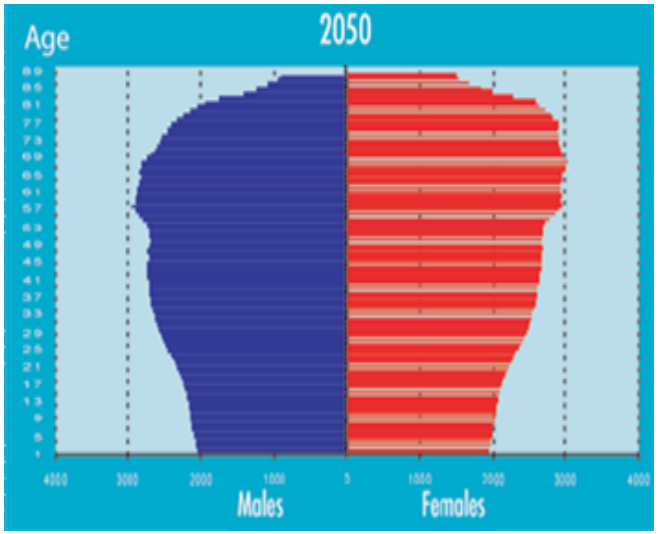
- Demographic challenge
- Stakeholder expectations
- EMA Roadmap to 2015
- CHMP workprogramme 2010-13
- Follow up to 2006 analysis

  requested by EC
- EU political agenda

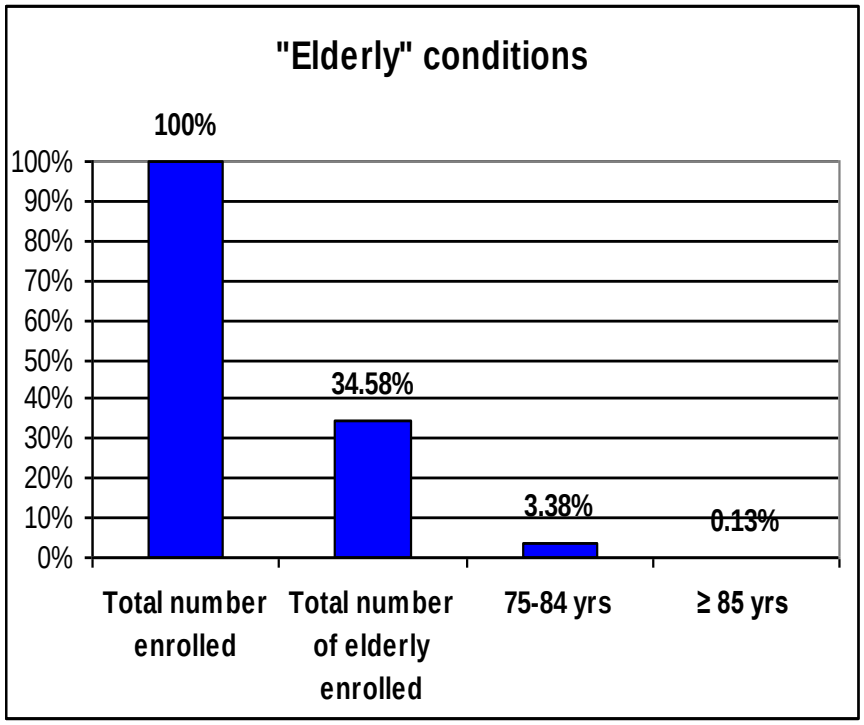
(parliament intergroup/2012

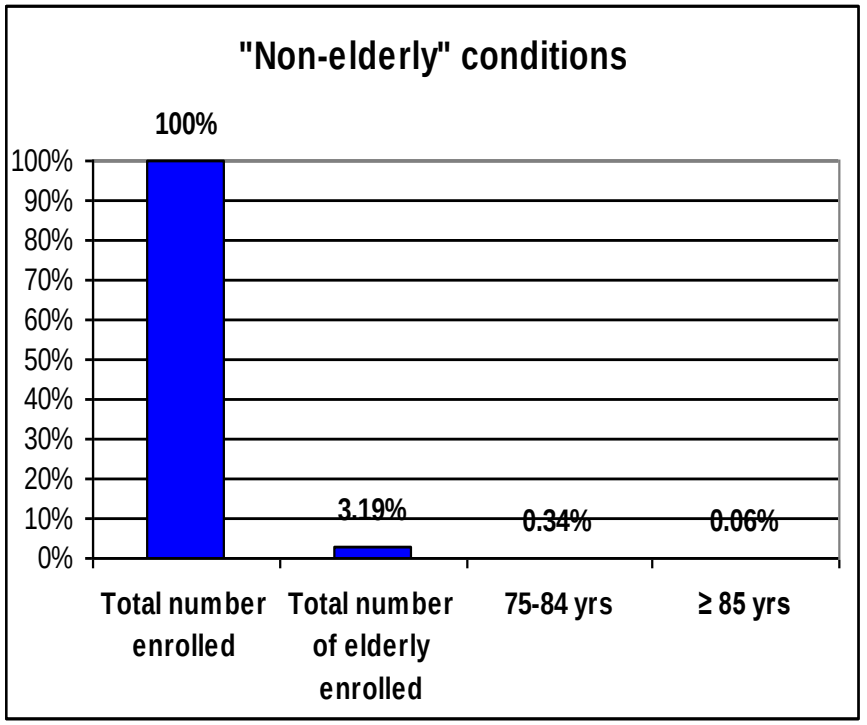
EU year of Active ageing/ EC Partnership)





Evidence Biased Medicine?
Initial findings mid-2009 to present: "elderly" *vs.* "non-elderly" conditions





EMA Vision for a geriatric strategy: TWO PRINCIPLES

Medicines used by geriatric patients must be of high quality, and appropriately researched and evaluated.. **for use in this population**.

⇨ Evidence based medicine

Improve the availability of **information** on the use of medicines for older people

⇨ Informed prescription

What about the benefit / risk balance in the older population?

- Is the benefit/risk demonstrated for the population that will use the product?
- Which studies have been carried out? Are they in line with current guidelines?
- Can relevant information be found in the EMA approval documents?
- What would prescribers, patients and HTA bodies like to know?

EMA Geriatric Medicines Strategy - Key points

1. "..ensuring that the development and evaluation of new medicines takes into account specific safety and efficacy aspects related to aging, in accordance with current guidelines, particularly ICH E7"
2. "..identifying gaps in regulatory and scientific knowledge and taking appropriate measures to tackle them"
3. "..consideration for the need of specific pharmacovigilance activities"
4. "..fostering and utilising a relevant experts' pool to address specific issues as requested by the CHMP."

Can we do better?

Two-pronged approach is needed to better use the tools we already have:

- Industry: follow guidelines. Discuss innovative solutions with the regulators
- Regulators: coordinate activities and improve communication to the patient and to the prescriber

!! No new processes !!

Changes to the CHMP AR

- Both AR templates and guidance
- Changes in line with the spirit of ICH E7
- Approved September 2011
- Published on website October 2011
- Aim is to focus attention of reviewer on geriatric data:
  - Amount
  - Context
  - Missing information

Changes to the CHMP AR (Efficacy)

- Include a clear description of epidemiology in relation to age within special populations
- Describe PK or discuss absence
- Need for dose adjustment discussed
- Demographic table:

	Age 65-74	Age 75-84	Age 85+
PK Trials	number /total number		
Controlled Trials			
Non Controlled trials			

Changes to the CHMP AR (Safety -2)

Following table included:

	Age <65 yrs	Age 65-74	Age 75-84	Age 85+
Total				
Fatal				
Serious				
Withdrawal				
CNS (confusion/extrapyramidal)				
AE related to falling				
CV events				
Cerebrovascular events				
Infections				

What do we need in the patient/prescriber information? (1)

SmPC 4.2 should provide specific information, dosage adjustment or precaution recommended in elderly population

BUT

Do not forget the PIL !!!!!!!!!!!!!

- The PIL is the most widely read of the documents we produce
- This is a vulnerable population (memory, font size, treatment compliance, cognitive impairment, dysphagia)
- This is a population less amenable to "modern" methods of getting information

What do we need in the patient/prescriber information? (2)

Provide significant information:

A: we know enough

- Reflect it clearly.
- Be relevant on:
  - Drug-drug and drug-disease interactions (cross refer)
  - Dose adjustment (cross refer)
  - Administration/ no crushing (cross refer)
  - Need for follow up foreseen in RMP

What do we need in the patient/prescriber information? (3)

Provide significant information:

B: we know SOMETHING but there are still uncertainties

- If we know a little, and have some reassurance that adult data can be bridged to elderly, we should state "only limited data have been provided…."
- Clarify: what are we missing to be sure of the B/R?
- "Use with caution" does it really help in making a prescribing decision? Is it an "easy way out"? What actions and precautions are needed?

What do we need in the patient/prescriber information? (4)

Provide significant information:

C: we know VERY little

- The SmPC is not the place to report non interpretable/actionable data (if sample is too small). Discussion on this goes in the EPAR.
- If we cannot conclude/advise = we do not know the B/R. And this should be clearly stated in the SmPC.

General Considerations

- Older people in many cases constitute the main users of a drug, not a special population.
- Older adults are underrepresented in clinical trials (relative to disease prevalence) but the situation seems to be improving.
- Following ICH E7 Q&A, a representative number of patients should be studied pre-authorisation.
- Data should be presented for the entire age spectrum

General Considerations (2)

- There is a learning curve to gather data and modulate risk
- Clinician often acts as gatekeeper in recruitment, and determines a selection bias by recruiting only some of the eligible patients
- Population PK or specific PK study including the very elderly should be performed and will help informed prescription

Endpoints - Considerations

Depending on frailty/disability the desirable outcome and treatment decisions might be different

Functional endpoints might be more relevant in certain cases (GEG input)

This may have HTA implications

Discuss in Scientific advice or parallel HTA/SA

Do we need to change the endpoints or the way we evaluate them?

Increasing recruitment - Considerations

Strategies and interventions to improve participation at level of ethic committees, recruitment process and trial conduct have been presented

- Communication & Logistics
- Make use of existing networks
- Feed back the results
- age exclusion should be justified,
- commonly prescribed co-medication in this population should be allowed;
- multimorbid patients should be allowed;
- trial sponsor should provide support measures to encourage recruitment;
- CT outcome measures should be relevant to old people.

Frailty and Older-old patients- Considerations

Consensus on Frailty definition and evaluation tools is needed (input from geriatric expert group GEG suggests SPPB)

More effort is needed to recruit patients 75+ in clinical trials: EFPIA survey shows preferred option is same clinical trial. Separate trial might be needed.

Accurate reflection of data in patients >75 years is important

EFPIA: comorbid patients should be in same Phase 3, However there is indication that a separate trial might be have better results in terms of recruitment

Data expected in the MAA, postmarketing will depend on target population- condition in RMP/Annex 2

Sarcopenia is a worthwhile clinical endpoint *per se* (frailty is predictor of clinical outcomes + global societal benefit)

Product information – Considerations

No good information is possible if there are no good data

Sometimes there is good information but not reflected

Channels of information are important- both to patient and prescriber

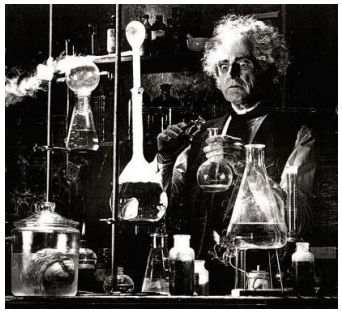
Better focus on Package leaflet

Specific measures are needed particularly as the older group is non homogeneous Better explain how to take medicine/increase compliance/PK and PD changes/concomitant medication

Consolidate in a comprehensive section?

information to Nurses should be allowed (?)

"Close loop drug product supply"



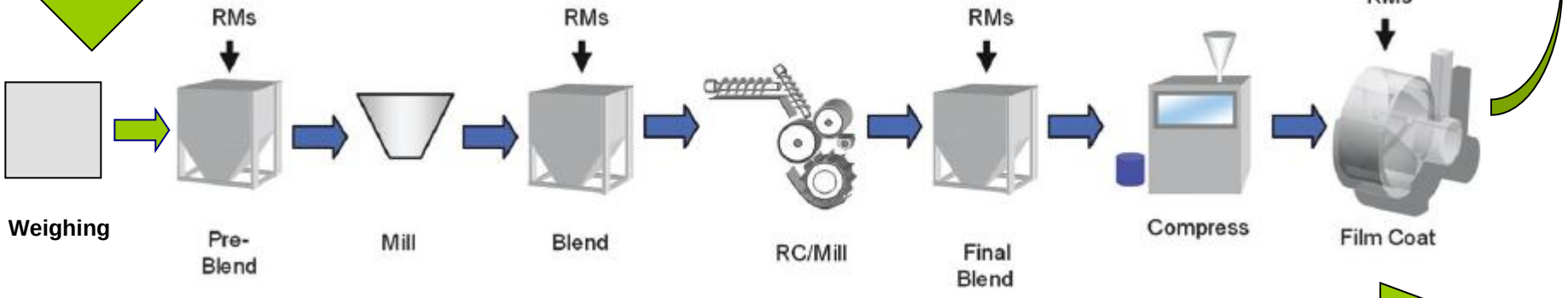
Formulation Development

Drug

Drug application

High quality pharmaceutical product

Process Development



Manufacturing

Formulations and Adherence – Considerations

Inappropriate formulations are conductive to low adherence and Safety and Efficacy problems

Multimorbidity/ dose reduction/ visual and mobility impairment needs to be considered when designing formulations

Issue probably more complex than paediatric due to variability in older population)

Protocols to evaluate the ability of patients to manage medication could be considered

QWP might take conclusions of workshop as starting points for a consultation on possible guideline on formulations (possible Q&A document)

Medication errors is an area where PRAC might seek QWP input

A Q&A on adherence aspects pertaining to Q/MI/PhV could be developed

Conclusions: how to strengthen pharmacovigilance

Risk management – based on the risk profile – plan to fill knowledge gaps through post-authorisation studies; targeted risk minimisation

Collection of data – optimise all possible data sources – facilitate reporting of suspected side effects, patient reporting; drug utilisation; electronic health records

Detecting new safety issues – huge potential to better use spontaneously reported adverse reactions: drug-drug and drug-disease interactions; focus on off-label use, medication errors, event clusters (e.g. falls dizziness);

Conclusions: how to strengthen pharmacovigilance 2

Evaluation of safety issues – always consider the elderly

Benefit risk evaluation – dedicated consideration of elderly population; specific patient values placed on benefits and risks

Regulatory action – consider targeted action

Communications – meet the information needs of the elderly; support decision-making; target communication and risk minimisation

Next steps (1)

Report in one year on strategy impact as compared to baseline

CHMP will continue to consider older population in assessment

Reporting of results in regulatory documents will need to be improved

When drafted or revised, CHMP will consider strengthening existing disease specific guidelines, with particular regard to older-old, comorbidities, frailty

Next steps (2)

Pharmacovigilance activities, based in particular on new legislative tools

QWP might take conclusions of workshop as starting points for a consultation on possible Q&A on formulations

Frailty: need to agree on scale(s) for regulatory purpose

Internal EMA Processes to consider age-appropriateness of formulations, packaging are being developed (both in SA and MAA

Thank you!

Questions?