EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The European Medicines Agency's review process of medicines' labelling and packaging to prevent risks of medication errors

IMSN Paris Satellite conference on safer naming, labelling and packaging of medicines – 10th October 2013

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An agency of the European Union

Introduction

- Legal Basis
- Product Information Quality Service
- Checking process of mock-ups and specimen of outer/immediate labelling and package leaflets
- Interactions with stakeholders
- Conclusions

Legal basis

European legislation:

- Title V of Directive 2001/83/EC.
  - **Art.54,55 and 59** lay down i**nformation** to appear on outer/immediate **packaging** and on **package leaflet**.
  - **Art.61** states that one or more **mock-ups** of **outer/immediate** packaging and **package leaflet** is **submitted** to the **Agency** when marketing authorisation is requested.
- Guideline on the readability of the labelling and package leaflet of medicinal products for human use. (Rev.1, January 2009)
  - Sets out helpful **advice** on the **presentation** of the **content** of the **labelling** and **package leaflet** and on the **design** and **layout** concepts to ensure that medicines can be used safely and appropriately.
- Guideline on the Packaging information of Medicinal Products for Human Use authorised by the Community" (Rev.14, July 2013)
  - Provides, in particular, information on the **requirements** by some **Member States** to appear on the outer packaging "**Blue Box**" (Art.57 of Directive 2001/83/EC).

Legal basis

- Checking process of Mock-Ups and Specimens of outer/immediate labelling and package leaflets of human medicinal products in the centralised procedure (Rev.1, March 2013).

  - **Review process** developed by the Agency in 2007 detailing the **checking** process of the **printed packaging materials** for outer/immediate **labelling** and **package leaflet** for centralised products.

- Product information Templates

  - Set out the **standard headings** and indicate the most commonly used **standard statements** and terms in all the official European Union **languages** (plus Norwegian and Icelandic).

Other reference documents:

- National Medicines Regulatory Agencies guidance.
- Publication and guidance published by organisations focused on patient safety and safe medication practice.
  - MHRA best practice guidance on labelling and packaging of medicines (June 2003)
  - Design for patient Safety: A guide to the graphic design of medication packaging (National Patient Safety Agency, UK) (Edition 2, 2007)

Product Information Quality (PIQ) Service

PIQ covers 3 main areas:

- Quality Review of product information (**content** and **linguistic** review of the **summary of product characteristics** (SmPC), the **labelling** and the **package leaflet**).
- Mock-ups & specimens of **outer/immediate labelling review** (**packaging layout and readability of information**).
- Name Review Group secretariat (Review of proposed **product names**).

=> Part of routine risk minimisation measures.

Key findings

- **Problems** with the **labelling and packaging** have been associated with a high number of medication errors.
- *The **labelling** and **packaging** ensures that the critical information necessary for the safe use of the medicines is **legible**, **easily accessible** and that users of medicines are assisted in assimilating this information so that **confusion** and **error** are **minimised****.*
- Correct identification/use of medicines relies on **good quality labelling**.

* Guideline on the readability of the label and package leaflet of medicinal products for human use.

Mock-Ups and Specimens review - **Definition**

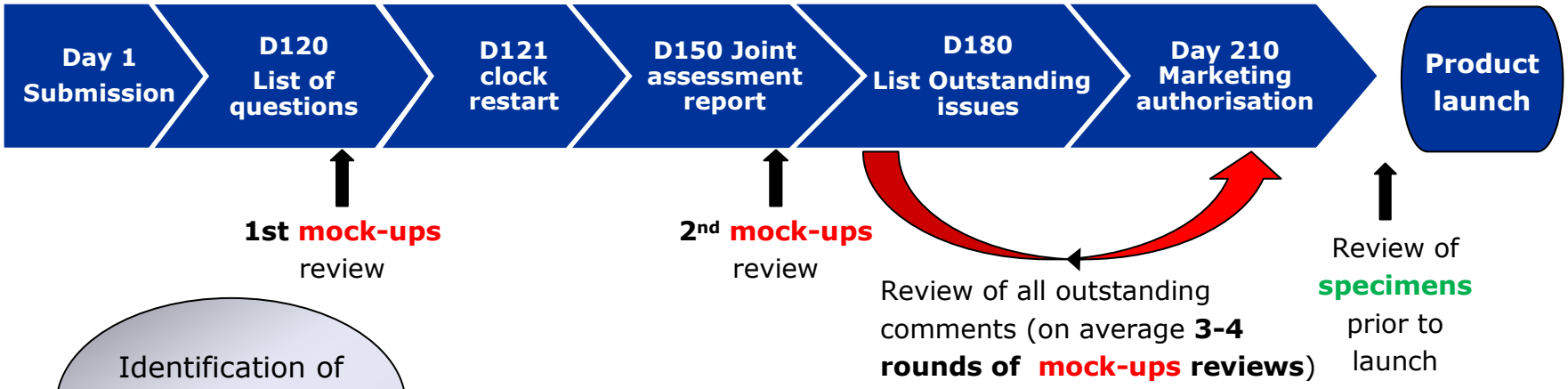
- **Mock-up**: copy of the flat artwork design in full colour (A3/A4 format).

- **Specimen**: samples of the actual printed outer and immediate packaging materials and package leaflet (i.e the sales presentation).

Mock-Ups and specimens review - **Procedure**

- **Mock-ups** are reviewed in **parallel** to the **scientifc assesment:**
  - Submission of **English** and **multi-lingual** ("worst case") colour mock-ups
  - For outer and immediate packaging
  - For each pharmaceutical form and strength
  - For each container type (e.g. blister, bottle, vial…etc.).
- **Specimens** reviewed **before launch:**
  - Submission of one set of the **relevant specimens** of outer and immediate packaging and package leaflet
  - To be provided for review at the latest **15 working days before launch**;
  - For each pharmaceutical form and strength
  - For each container type (e.g blister, bottle, vial…etc.).

Mock-Ups and specimens review – **Timeline (New applications and extensions)**



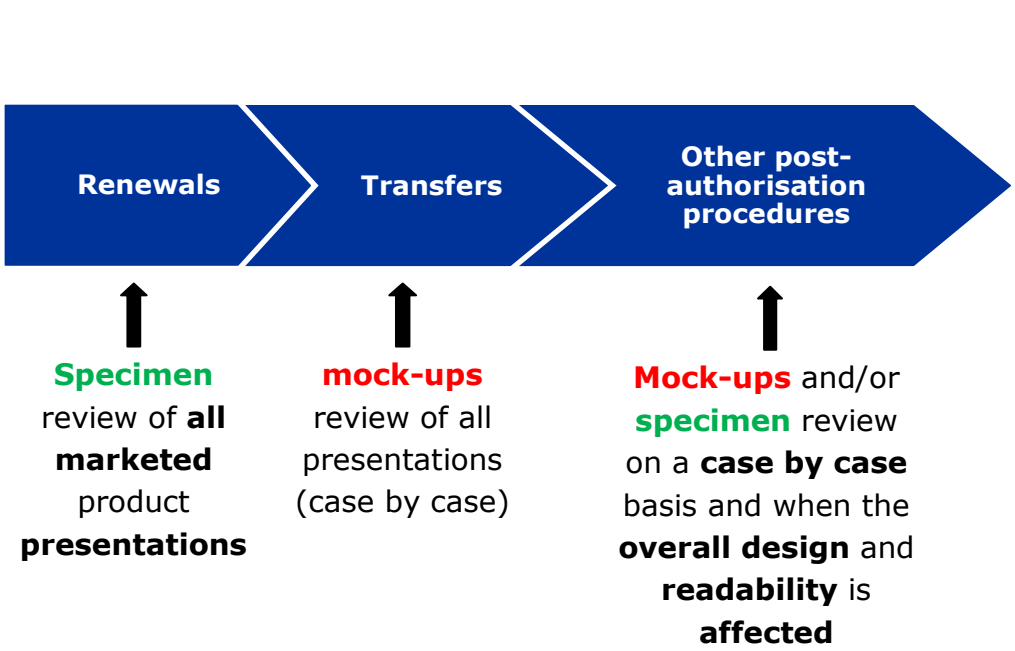
Identification of issues at an early stage

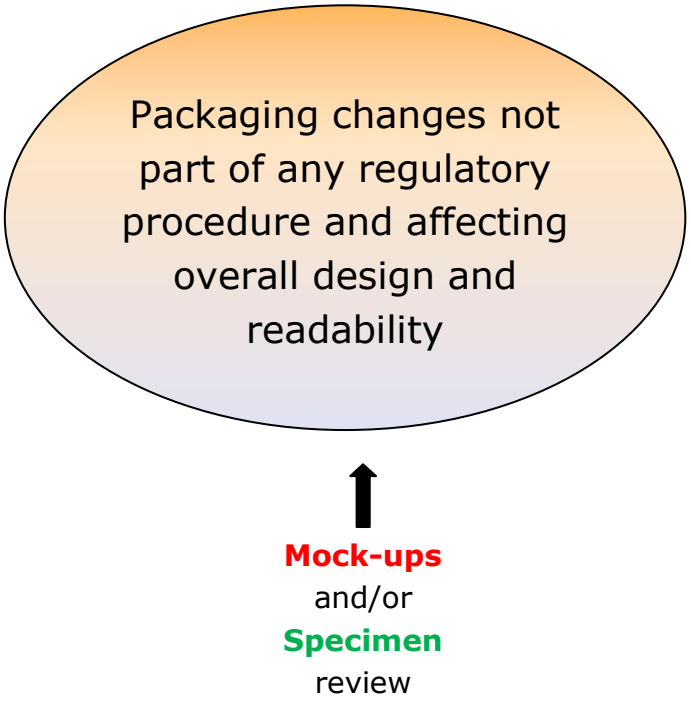
Liaise with assessors

Liaise with experts

Changes to labelling prior to specimen printing – shorter specimen reviews – facilitate faster launch

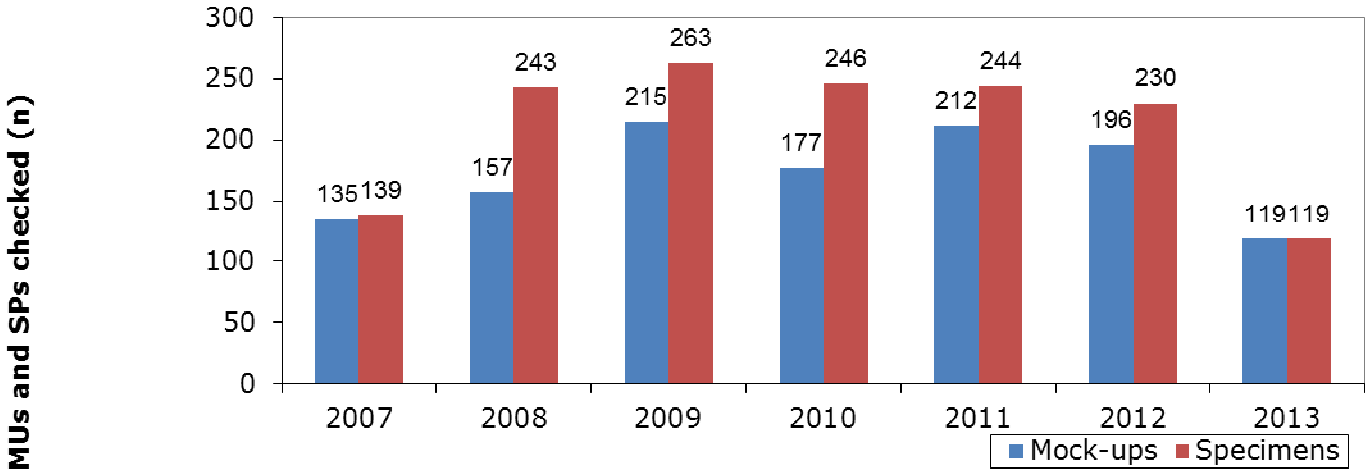
Mock-Ups and specimens review – **Timeline (post-authorisation procedures)**





Mock-Ups and Specimens review – **Who** is checking?

- We are a small team.
  - Some statistics (2007 to July 2013)*:



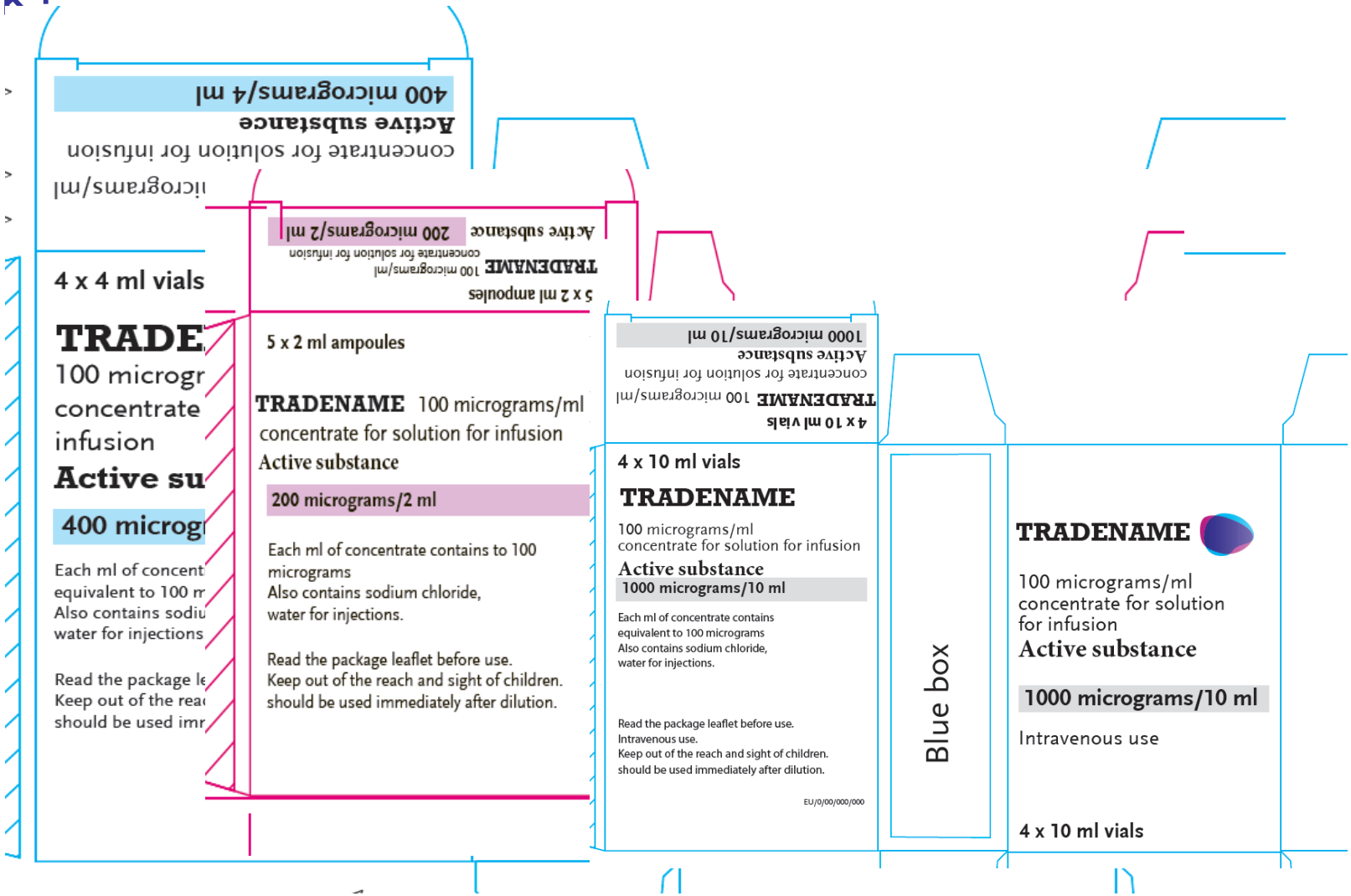
*based on number of reviews.

Mock-Ups and Specimens review – **What** do we check?

- General check from the **viewpoint** of **readability*:**
  - Ensure that the **critical/important information** for the safe use of the medicine is **legible** and clearly mentioned on **prime spaces** of the labelling to minimise the occurrence of medication errors.
- **Focus**:
  - Presentation of critical information (name of medicine, strength/concentration, pharmaceutical form and active substance)
  - Special warnings
  - Differentiation between strengths
  - Font sizes, positioning of the text , line spacing
  - Use of colours/pictograms/logos
  - Overall lay-out and design

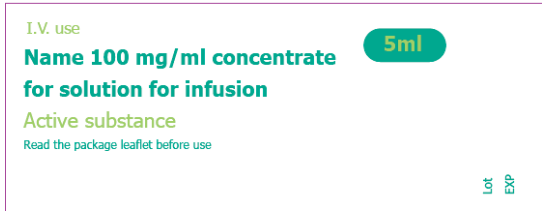
* No detailed linguistic check (i.e. no checking of the actual text.)

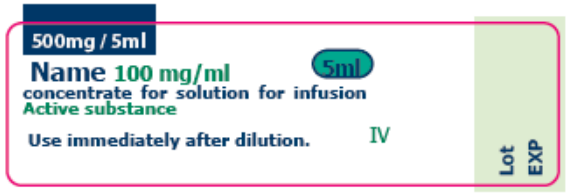
Mock-Ups and Specimens Review – **How** do we check?

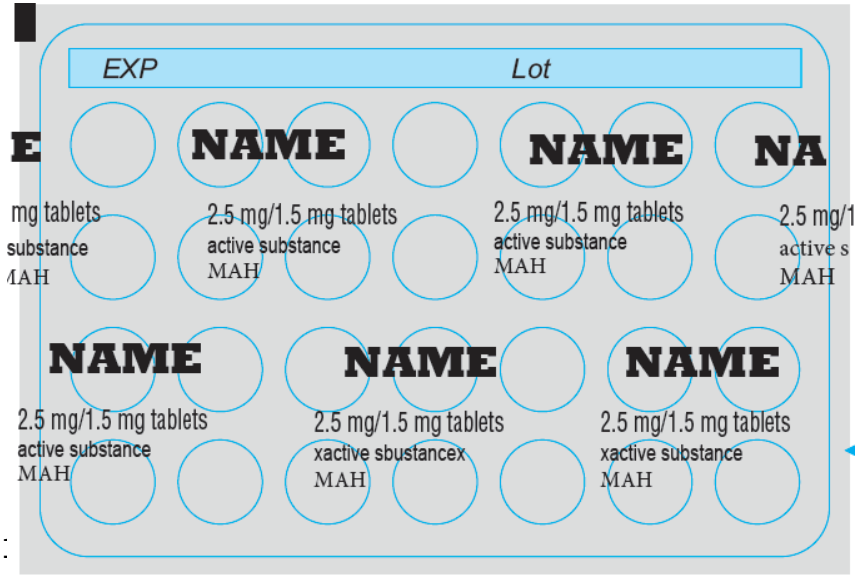


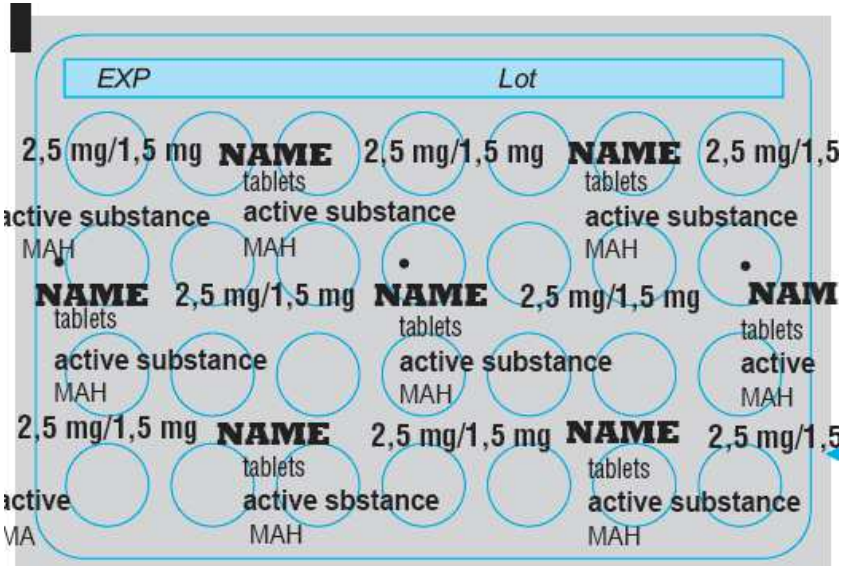
Mock-Ups and Specimens Review – **Example**

Mock-Ups and Specimens Review – **Examples**









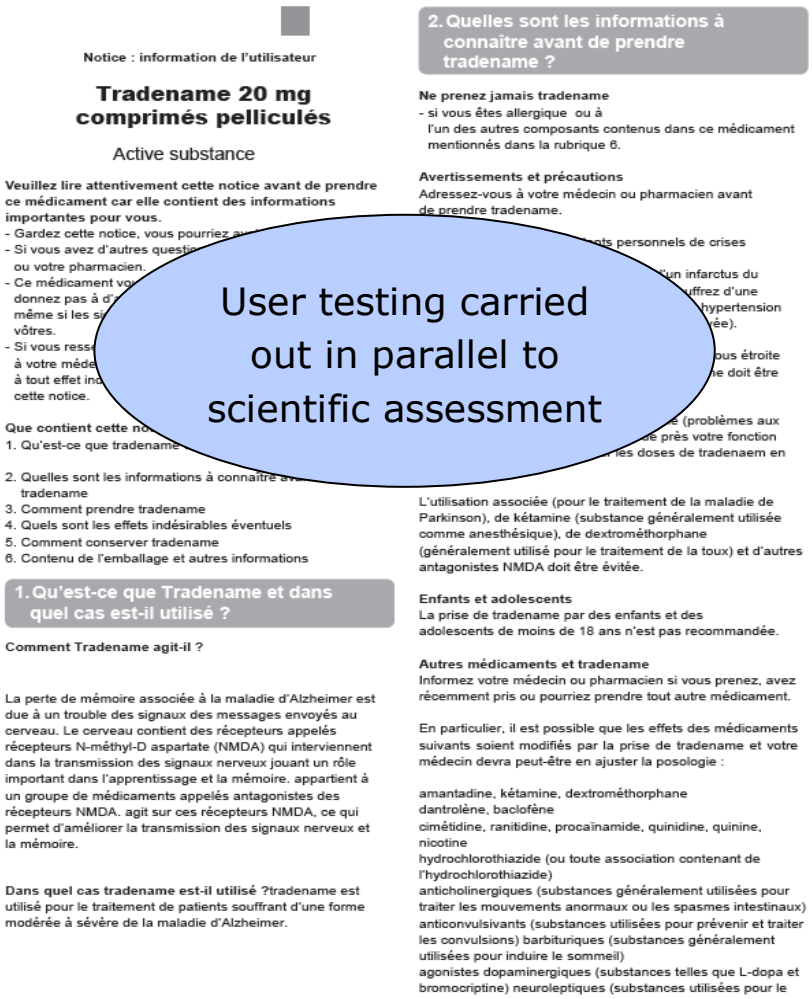
Mock-Ups and Specimens Review – **How** do we check? – **Package leaflets**

Clear headings to help navigation

Folds not interfering with text readability

Use non-glossy paper

Length of the leaflet



Notice : information de l'utilisateur

Tradename 20 mg comprimés pelliculés

Active substance

Veuillez lire attentivement cette notice avant de prendre ce médicament car elle contient des informations importantes pour vous.
- Gardez cette notice, vous pourriez
- Si vous avez d'autres questi
ou votre pharmacien.
- Ce médicament vo
donnez pas à d
même si les s
vôtres.
- Si vous ress
à votre méde
à tout effet in
cette notice.

Que contient cette no
1. Qu'est-ce que tradename
2. Quelles sont les informations à connaître av
tradename
3. Comment prendre tradename
4. Quels sont les effets indésirables éventuels
5. Comment conserver tradename
6. Contenu de l'emballage et autres informations

1. Qu'est-ce que Tradename et dans quel cas est-il utilisé ?

Comment Tradename agit-il ?

La perte de mémoire associée à la maladie d'Alzheimer est due à un trouble des signaux des messages envoyés au cerveau. Le cerveau contient des récepteurs appelés récepteurs N-méthyl-D aspartate (NMDA) qui interviennent dans la transmission des signaux nerveux jouant un rôle important dans l'apprentissage et la mémoire. appartient à un groupe de médicaments appelés antagonistes des récepteurs NMDA. agit sur ces récepteurs NMDA, ce qui permet d'améliorer la transmission des signaux nerveux et la mémoire.

Dans quel cas tradename est-il utilisé ?tradename est utilisé pour le traitement de patients souffrant d'une forme modérée à sévère de la maladie d'Alzheimer.

2. Quelles sont les informations à connaître avant de prendre tradename ?

Ne prenez jamais tradename
- si vous êtes allergique ou à l'un des autres composants contenus dans ce médicament mentionnés dans la rubrique 6.

Avertissements et précautions
Adressez-vous à votre médecin ou pharmacien avant de prendre tradename.

nts personnels de crises

un infarctus du
uffrez d'une
hypertension
vée).

ous étroite
e doit être

é (problèmes aux
e près votre fonction
les doses de tradenaem en

L'utilisation associée (pour le traitement de la maladie de Parkinson), de kétamine (substance généralement utilisée comme anesthésique), de dextrométhorphane (généralement utilisé pour le traitement de la toux) et d'autres antagonistes NMDA doit être évitée.

Enfants et adolescents
La prise de tradename par des enfants et des adolescents de moins de 18 ans n'est pas recommandée.

Autres médicaments et tradename
Informez votre médecin ou pharmacien si vous prenez, avez récemment pris ou pourriez prendre tout autre médicament.

En particulier, il est possible que les effets des médicaments suivants soient modifiés par la prise de tradename et votre médecin devra peut-être en ajuster la posologie :

amantadine, kétamine, dextrométhorphane
dantrolène, baclofène
cimétidine, ranitidine, procaïnamide, quinidine, quinine, nicotine
hydrochlorothiazide (ou toute association contenant de l'hydrochlorothiazide)
anticholinergiques (substances généralement utilisées pour traiter les mouvements anormaux ou les spasmes intestinaux)
anticonvulsivants (substances utilisées pour prévenir et traiter les convulsions) barbituriques (substances généralement utilisées pour induire le sommeil)
agonistes dopaminergiques (substances telles que L-dopa et bromocriptine) neuroleptiques (substances utilisées pour le

User testing carried out in parallel to scientific assessment

Critical information in bold

Font size readability

Use of non-justified text

Contrast between text and background (Paper weight and colour)

Mock-ups and Specimens review – **Challenging areas**

- **Family design**

  - Similarity issues due to:

    - Use of same design
    - Use of defined colour coding
    - Same colour patterns used for different combinations of active substances.
    - Strengths and active substance or combinations of active substances not prominent enough

- **Pack design** is an **important** element of **patient safety** and **companies** should ensure that all their **products using a family design** are **identifiable** and are easily **differentiated** between them.

Mock-ups and Specimens review – **Challenging areas**

Information has to be identical in all the languages

28 Member States (+ IS and NO)

25 languages

Multilingual packaging

Tri-lingual packaging legal requirement (Belgium)

Bi-lingual packaging legal requirement (Finland)

All languages packaging (e.g. orphan medicines)

Different languages combination can be used

Size of the packaging might allow inclusion of many languages

Mock-Ups and Specimens Review – **Multilingual packaging**

- All these readability principles can be **very difficult to apply on multilingual packaging.**

- The general readability is affected by the **decrease** of the **font size**, **dense blocks** of text, less **line spacing** and **less prominence** of the critical information.

⇒ The **same principles** applied to the single language packaging are **valid**.

⇒ The **readability** and the **clear** and **unambiguous** identification of the medicine should be ensured.

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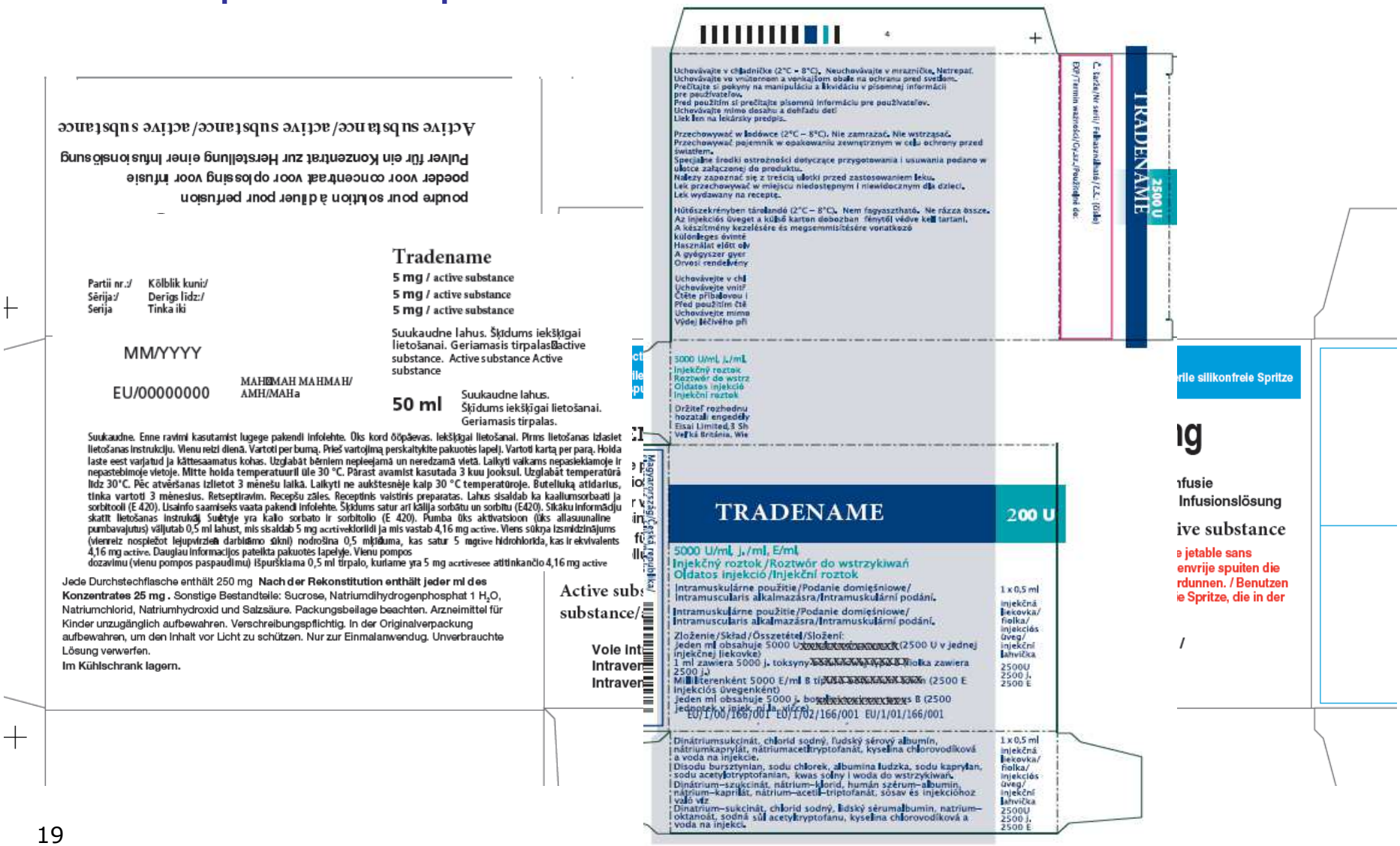
Mock-Ups and Specimens Review – **Examples**



Mock-Ups and Specimens Review – **Multilingual packaging**

- **Several strategies are available:**

➢ Use of innovative labels

  ➢ Display of one language per panel

  ➢ Use of English or Latin for the active substance

  ➢ Use of short standard terms (pharmaceutical form, route of administration, container)

  ➢ Use of standard abbreviations

  ➢ Text simplification (Art.63 of Directive 2001/83/EC)*

  ➢ Language exemption (Art.63 of Directive 2001/83/EC)*

  ➢ To have thorough assessment of the text that will be displayed

*Products not intended to be delivered directly to the patient and orphan products

Mock-Ups and Specimens Review– **Availability issues**

- **Labelling** can be **one of the main obstacles** preventing marketing of medicines in **small markets**.

- Need to **balance** between **multilingual** packaging **restrictions** and **availability:** patients, physicians, pharmacists need medicines.

  ⇒ Need to **develop guidance for multilingual** labelling.

  ⇒ All available **guidance** usually **refers** to **single-language** packs leading to request for **text simplification** to accommodate multilingual packs.

  ⇒ Text simplification **raise concerns** amongst some **Member States** where single language packs are used.

Mock-Ups and Specimens Review– **Interactions**

Who do we involve?

Patients and Consumers

Healthcare professionals

Patient safety and safe medication practices organisations

Member States

Mock-Ups and Specimens Review– **Interactions**

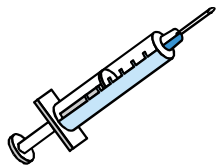
- As part of the **routine risk minimisation measures**, the Agency reviews:
  - Statutory information included in the **product information** (Summary of product characteristics (SmPC), the labelling and the package leaflet)
  - Readability of the **packaging**
- However, sometimes there is also scope to further address the **practical aspects** of prescribing, dispensing and handling of the medicine to prevent potential medication errors.

Need for expertise

Mock-Ups and Specimens Review– **Interactions**

- **Member States, patients** and **healthcare professionals** are consulted during the product information and the packaging review:

  - **Member states (Quality Review of Document (QRD) group)**
    - Review of the product information (Linguistic review process)
    - On a case by case basis review of the packaging
  - **Patients:**
    - Review of the package leaflet
    - On a case by case basis review of the packaging
  - **Healthcare professionals**
    - Consulted when specific expertise is required (product information, packaging, educational material…etc.).



Mock-Ups and Specimens Review– **Interactions**

- The following are **some** of the **areas** were **Member States, Patients,** and **Healthcare professionals** were **consulted**:
  - Introduction of a new **device**/change of device
  - Introduction of a new **pharmaceutical form**
  - Inclusion of specific **warnings**
  - Introduction of a new **concentration**/new **strength**
  - Review of layout and **readability** in the context of **multilingual** labelling
  - Confusion due to unclear **instructions for use**
  - **Expression of strength** issues (e.g. injectable)
  - Qualitative & quantitative composition – **active substance** (*salt* vs. *base*)
  - Completeness of **package leaflet** compared to SmPC
  - Labelling **simplification** (Art.63)
  - Potential for **medication errors**

Mock-Ups and Specimens Review– **Interactions**

- Our **experience** showed that the **biggest improvements** to the labelling/packaging were the **results** of the **collaboration** with healthcare professionals, patients and patient safety and safe medication practice organisations.
- Need to **strengthen** the **links** with all **stakeholders**.
- Especially work closely with **Patient safety and safe medication practices organisations**.

➢ **Respond** to reports from Patient safety and safe medication practices organisations (post-marketing):

  - Dosing errors reported due to expression of strength (Torisel)
  - Dosing errors reported due to active substance expressed as *base* rather than *salt* (Halaven)

Conclusions

- The correct identification/use of medicines relies on **good quality labelling**.
- The establishment of an **interaction** with **stakeholders** in the area of the **review** of the **labelling/packaging** is **important** in the prevention of medication errors.
- Further **collaboration** with stakeholders, **including industry**, to develop Safety guidelines on labelling and packaging is **crucial**.
- Despite the **challenges**, we are making **significant progress** in this area.
- The **Agency** is **committed** to **actively engage** with national competent authorities, patients, consumers, healthcare professionals, patient safety and safe medication practices organisations and industry **to tackle the issue of medication errors.**

Contacting the Agency

- For any queries related to the review of mock-ups and specimens:
  muspecimens@ema.europa.eu

- For any queries related to the work of the Agency:
  info@ema.europa.eu

www.ema.europa.eu

Grazie!

Merci!

Thank you!