EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# Article 8 – Paediatric Regulation

Interpretation of pharmaceutical form

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# Article 8 – Reg. (EC) No 1901/2006

*In the case of authorised medicinal products which are protected either by a supplementary protection certificate under Regulation (EEC) No 1768/92, or by a patent which qualifies for the granting of the supplementary protection certificate, Article 7 of this Regulation shall apply to applications for authorisation of new indications, including paediatric indications,* ***new pharmaceutical forms*** *and new routes of administration.*

# What is a new pharmaceutical form?

- No legal definition

- EDQM – Standard Terms
  - Classification list
  - Form of administration + Form of presentation
  - Sometimes very detailed: solvent, container

# Application to Registration procedures – Different references!

- Line extension vs variations - Guideline on categorisation (2003)
- Generics: 'same pharmaceutical form' - Directive 2001/83/EC + ECJ - C-106/01, Novartis
- Naming: Standard Terms
- Annex A of centralised MA: ST minus container
- Article 8 paediatrics?

# No perfect solution!

1) At least be consistent between :

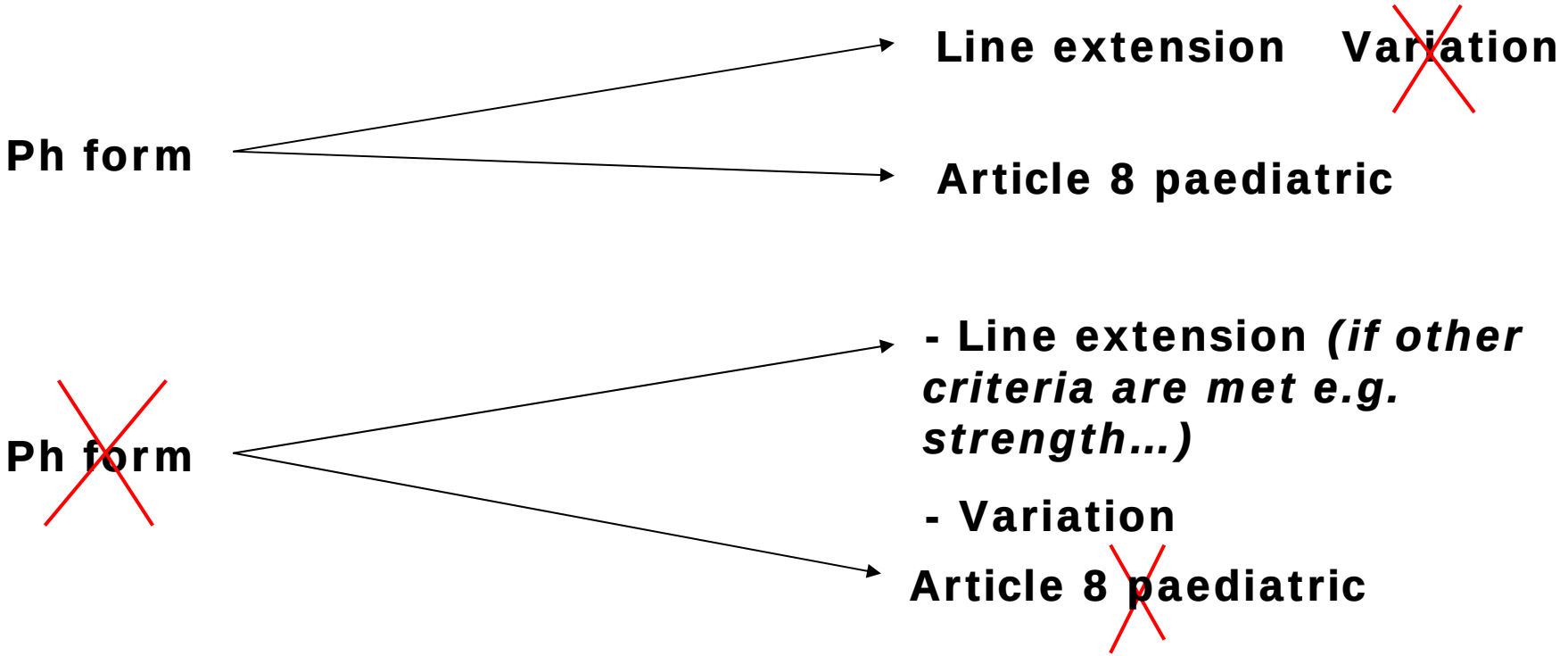
QUALITY: line-extension or variation

And

PAEDIATRICS: art.8 or not

2) And try to find a proportionate interpretation

# EMA Position – Consistency between procedures




**Article 2(4)**

*"'Extension of a marketing authorisation' means a variation which is listed in Annex I and fulfils the conditions laid down therein"*

**Annex I**

*"(…) 2. Changes to strength, pharmaceutical form and route of administration:(…)*
*(d) change or addition of a new pharmaceutical form"*

# EMA Position – How defining internally the PF?

1. Standard Terms remains the reference – change=PF
   - Immediate-release to modified-release
   - Solution for injection to solution for infusion

2. however possibility of variation - not new PF - according to the guideline on classification for:
   - Change of immediate container (pre-filled syringe / pen / cartridge / vial…)
   - Deletion of solvent
   - Change in the administration device (applicator,…)

# In practice, no PF (if accepted as variation)

| | |
|---|---|
| **Change in the current Standard Terms/Combined Terms:** | - Immediate container (pre-filled syringe / pen / cartridge / vial…)<br>- Solvent<br>- Devices for facilitating the administration (applicator,…) |
| **No Change in the current Standard Terms/Combined Terms:** | - Immediate container (blister, bottle,…)<br>- devices for facilitating the administration (empty syringe, empty oral syringe, swab,…)<br>- devices for facilitating the reconstitution (transfer kit,…) |

# Examples

- Addition of a solvent
- Introduction of a pre-filled syringe in addition to the current vial and *vice versa*
- Addition of a pre-filled pen (cartridge) to the current pre-filled syringe
- Addition of a pre-filled syringe instead of a vial for the solvent ("Powder (in vial) and suspension (in vial) for suspension for injection" to "*Powder (in vial) and suspension (in pre-filled syringes) for suspension for injection")*

# Variations – Guideline on classification - 02/2010

***B.II.e.1*** *- Change in immediate packaging of the finished Product*

***B.IV.1*** *- Change of a measuring or administration device*

*a) Addition or replacement of a device which is not an integrated part of the primary packaging*

*- Device with CE marking*

*- Spacer device for metered dose inhalers*

*b) Deletion of a device*

*c) Addition or replacement of a device which is an integrated part of the primary packaging*

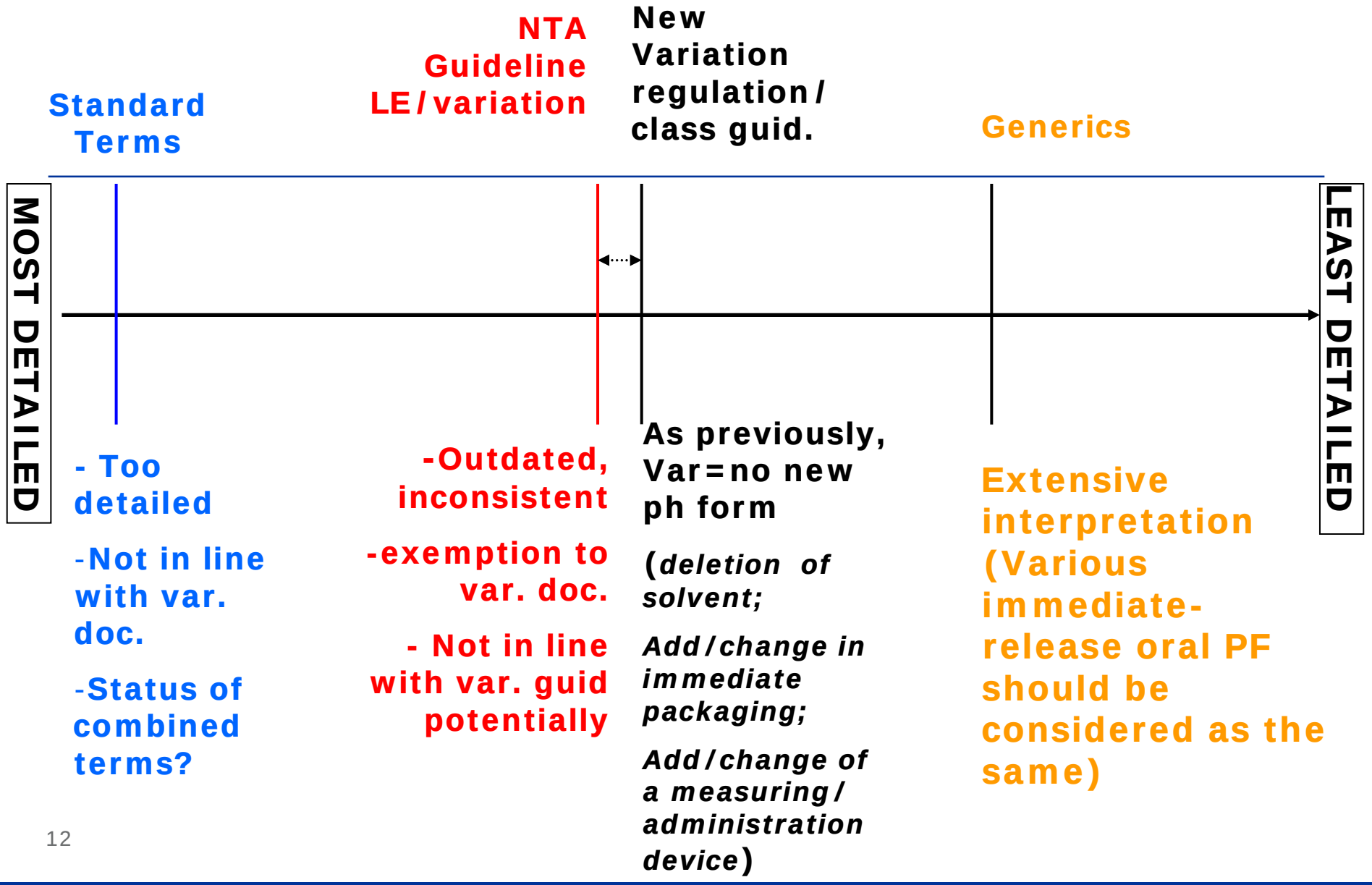
***B.II.a.6*** *- Deletion of the solvent / diluent container from the pack*

| **Parenteral preparations**<br>**(change from the left hand column to the right hand column and vice versa)** | |
|---|---|
| Powder and solvent for solution for injection in **pre-filled syringe** | Powder and solvent for solution for injection |
| Powder and solvent for solution for injection in **pre-filled syringe** | Powder and solvent for solution for injection in **vial** |
| Solution for injection in **cartridge** | Solution for injection |
| Solution for injection in **cartridge** | Solution for injection in **pre-filled pen** |
| Solution for injection in **pre-filled pen** | Solution for injection in **pre-filled syringe** |
| Solution for injection in **pre-filled pen** | Solution for injection |
| Solution for injection in **pre-filled syringe** | Solution for injection |
| Solution for infusion in **pre-filled syringe** | Solution for infusion |
| Suspension for injection in **cartridge** | Suspension for injection in pre-filled syringe |
| Suspension for injection in **cartridge** | Suspension for injection |
| Suspension for injection in **pre-filled pen** | Suspension for injection |
| Suspension for injection in **pre-filled syringe** | Suspension for injection |
| Powder and **solvent** for solution for injection | Powder for solution for injection |

| **Oral preparations**<br>**(change from the left hand column to the right hand column and vice versa)** | |
|---|---|
| Granules and **solvent** for oral suspension | Granules for oral suspension |

| **Eye preparations**<br>**(change from the left hand column to the right hand column and vice versa)** | |
|---|---|
| Eye drops, solution *(unpreserved)* | Eye drops, solution in **single-dose container** *(preserved)* |

| **Cutaneous and transdermal preparations**<br>**(change from the left hand column to the right hand column and vice versa)** | |
|---|---|
| Powder and **solvent** for cutaneous solution | Powder for cutaneous solution |
| Concentrate and **solvent** for cutaneous solution | Concentrate for cutaneous solution |
| Concentrate and **solvent** for cutaneous use | Concentrate for cutaneous use |


Standard Terms
NTA Guideline LE/variation
New Variation regulation/ class guid.
Generics
MOST DETAILED
LEAST DETAILED
- Too detailed
-Not in line with var. doc.
-Status of combined terms?
-Outdated, inconsistent
-exemption to var. doc.
- Not in line with var. guid potentially
As previously, Var=no new ph form
(deletion of solvent;
Add/change in immediate packaging;
Add/change of a measuring/ administration device)
Extensive interpretation (Various immediate-release oral PF should be considered as the same)