Regulation on medicinal products for paediatric use

ANWALTSKANZLEI STRÄTER

Burkhard Sträter

Kronprinzenstraße 20
53173 Bonn
Tel.:++49-228-93454-0
Fax.:++49-228-93454-54
Mail@kanzleistraeter.de
www.KanzleiStraeter.de

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Regulation on medicinal products for paediatric use

Findings: approx. 50 % off-label use in paediatrics

à Neonates à 100 %

à Children up to 18 years of age
à usual off-label use

Solution: à more paediatric research

à adjustment of the marketing authorisations

à by compulsion + incentives

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Market:	**MP protected by patent or SPC**	**Orphan medicinal products**	**MP with known substances**
	↑	↑	↑
	Special importance	**Special significance for serious diseases in children**	**Significant because known and safe**
	à Incentive by patent extension	**à Incentive by extending market exclusivity**	**à Incentive by data protection**

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Regulation on medicinal products for paediatric use 1901/2006/EC

creates:

- **à New procedure for approval of a paediatric investigation plan**
- **à Duty to research with the sanction of a marketing authorisation ban**
- **à Duty to distribute in favour of children**
- **à Incentive system through patent extension, extension of market exclusivity and data protection**

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Regulation on medicinal products for paediatric use 1901/2006/EC

changes:

à Regulation 1768/92/EC
- comprehensively to create or extend protection certificates

à Directive 2001/20/EC - Art. 11
– Publication of paediatric clinical trials

à Directive 2001/83/EC - Art. 6
– Distribution of medicinal products in the EU only if national, decentralised or centralised marketing authorisation exists and the Regulation on medicinal products for paediatric use is satisfied

à Regulation 726/2004/EC - Art. 56
Establishment of a Paediatric Committee at the EMEA

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Regulation on medicinal products for paediatric use

Duties of the pharmaceutical entrepreneur:

- Paediatric investigation plan

- Approval from the Paediatrics Committee/EMEA

- Conduct of studies in compliance with the investigation plan

Consequence:

Art. 7: refusal to grant new marketing authorisation if studies are not in compliance with the investigation plan

à Ban on marketing authorisation also for adults

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Duties: **Which medicinal products ?**

Art. 7 in principle: all new marketing authorisations

Art. 8 Line extensions if

à SPC or patent exists that comes into question

Art. 30 Authorisation for paediatric use – PUMA – only if trial is in compliance with the investigation plan (Art. 30 No. 2)

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Duties: **Which medicinal products ?**

Exceptions: **Art. 9**

à Generics

à Bibliographical applications - WEU

à Homeopathic agents

à Trad. phytopharmaceuticals

Art. 11 Waiver: **à Group, e.g. geriatrics and individual cases**

Art. 20 Deferral: **à first adults, then children**

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Paed. investigation plan - Application (Art. 15 et seq.)

procedure (Art. 18, 25 et seq.)

Approval by Paediatric Committee (Art. 6)

- Waivers (Art. 11)

Groups	Individual case
e.g. geriatrics	e.g. no benefit

- Deferrals (Art. 20)

Requirement: trial according to investigation plan
not a specific result

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Transitional provisions for **duties of the pharmaceutical entrepreneur**

Art 57:

- à Art. 7 (i.e. ban on marketing authorisation) applies 18 months after coming into force
- à Art. 8 (i.e. ban on marketing authorisation for patent-protected line extensions) applies 24 months after coming into force
- à Art. 31 (i.e. decentralised PUMA application)
  Art. 32 (i.e. labelling as paediatric medicinal product) applies 6 months after coming into force

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Regulation on medicinal products for paediatric use

Transitional provisions for duties of the pharmaceutical entrepreneur

Consequences arising from Art. 57:

à Deferrals for the end of research in the investigation plan are mandatory if "PIP compliance" is to be achieved when filing application from 2007.

The latter is mandatory pursuant to Art. 7, 8 and pursuant to Art. 28 (3) in connection with Art. 36 a prerequisite for incentives.

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Duties after granting approval:

Art. 33
Duty to distribute within two years of marketing authorisation

à in the case of marketing authorisation according to approved investigation plan

à incorporation in the EMEA Register

Art. 34
Vigilance by authorities and pharmaceutical entrepreneur

Art. 35
Discontinuation of distribution?

® **Duties:**

- **Notification to EMEA**
- **Transfer of the marketing authorisation to other pharmaceutical entrepreneurs**

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Incentives for Paediatric Research I
Concept of the EU-Commission

Regulation on MP for paediatric use - PU -

MP protected by patent or SPC

↓

6 months extension

if studies conducted in compliance with PIP

Art. 36

Orphan MP market exclusivity

↓

2 years extension

if studies conducted in compliance with PIP

Art. 37

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Incentives for Paediatric Research II
Concept of the EU-Commission

Paediatric Use Marketing Authorisation

⇨ **PUMA**

- MP not protected by patent or SPC
- MA exclusively for paediatric use, incl. strength, pharmac. form, rate of admin.
- If studies conducted in compliance with PIP

Art. 30

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Incentives for Paediatric Research III

Regulation for MP on PU

→ **Data protection** **~ Art. 10 Dir. 2001/83/EC**

~ Art. 14 (11) Reg. 726/2004/EC

→ **8 + 2 + 1 (non interim regulation!)**

→ **Protection for a line extension**

It may retain the name of

the original (Art. 30 (4)

Art. 38

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Proof of „PIP-Compliance“

requirement for all incentives!

Proof: Art. 28 Abs. para 3 **à all measures of PIP fulfilled**

à study results in SmPC labelled

à assessment in MA procedure

à confirmation in the approval-letter – expressly

à at what point in time is an „PIP-compliant“ application possible - earliest?

à Interim rules

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Proof of „PIP-Compliance“

sequence:

1. draft - PIP

à application for approval July/August 2007 earliest

2. authorisation procedure

à duration 3 – 6 months

3. start and end of the trials

à duration ?

4. approval in the MA procedure

à Art. 28 para 3

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Proof of „PIP-Compliance“

relevance for Art. 7 + 8 (Ban on MA)

à Art. 7 (Ban on MA) comes into force after 18 months

à Art. 8 (Ban on MA for patent-protected line extensions) comes into force after 24 months

à Art. 31 PUMA-application in centralised procedure
Art. 32 labelling as paediatric MP comes into force after 6 months

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Proof of „PIP-Compliance“

Art. 57 interim rule à consequences

à deferrals in PIP are required to gain PIP compliance for applications after July 2008

à PIP compliance is mandatory for MA applications (Art. 7 + 8) and

à requirement for incentives Art. 36 – Art. 28 para 3

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Incentives for Paediatric Research IV

Labelling:

Identification

- **MP authorised for paediatric use in compliance with PIP**
- **all others authorised for paediatric use**

The Commission will publish a symbol recommended by the Paediatric Committee to be labelled on each pack of MP authorised for paediatric use

→ **Labelling obligatory 2 years after publication of the symbol**

Art. 32

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Regulation on medicinal products for paediatric use
Rewards and incentives Art. 36 et seq.

Art 36 (3):

- **for DP + MRP: duty to grant marketing authorisation in all Member States**
- **for centralised authorisation ® applies in all EU MS by law**

Art 37:

- **for orphan MP ® duty to use the centralised procedure**

➡ **De facto compulsion to use the centralised procedure? Increased pressure at all events!!**

® **Art. 31 permits use of the centralised procedure irrespective of the qualifying features in Art. 3 of EC Regulation 726/2004**

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Transitional provisions for incentives + existing studies

Art 45: - existing studies must be submitted

- consideration in investigation plan and in the marketing authorisation (+)

but Art. 45 (3):

Rewards and incentives only if:

- **completion of**
- **significant studies**
- **approved in a PIP**
- **after regulation comes into force**

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Transitional provisions for incentives **+** existing studies

Patents Agency will request proof of significance, Art. 36 (2) and Art. 37 make reference to Art. 28 (3)

⇨ **The significance is determined in a binding manner in the marketing authorisation and in the notice of marketing authorisation. This is a prerequisite for granting rewards.**

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Thank you for your attention!

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