The EU Revised Class Waiver list

Gilles Vassal

Amsterdam, 2018

European Commission

Better Medicines for Children From Concept to Reality

PROGRESS REPORT ON THE PAEDIATRIC REGULATION (EC) N°1901/2006

COM (2013) 443
FINAL

REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 12 December 2006

on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

Article 11

1. Production of the information referred to in point (a) of Article 7(1) shall be waived for specific medicinal products or for classes of medicinal products, if there is evidence showing any of the following:

(a) that the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part or all of the paediatric population;

(b) that the disease or condition for which the specific medicinal product or class is intended occurs only in adult populations;

(c) that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

LIST OF CONDITIONS WAIVED

- Treatment of oropharyngeal, laryngeal or nasal epithelial carcinoma (excluding nasopharyngeal carcinoma or lymphoepithelioma)
- Treatment of lung carcinoma (small cell and non-small cell carcinoma)
- Treatment of basal cell carcinoma
- Treatment of breast carcinoma
- Treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours)
- Treatment of Fallopian tube carcinoma (excluding rhabdomyosarcoma and germ cell tumours)
- Treatment of endometrial carcinoma
- Treatment of peritoneal carcinoma (excluding blastomas and sarcomas)
- Treatment of prostate carcinoma (excluding rhabdomyosarcoma)
- Treatment of hairy cell leukaemia
- Treatment of multiple myeloma
- Treatment of Alzheimer's disease
- Treatment of vascular dementia and vascular cognitive disorder/impairment
- Treatment of organic amnesic syndrome (excluding amnesic syndrome caused by alcohol and other psychoactive substances)
- Treatment of amyotrophic lateral sclerosis
- Treatment of Parkinson's disease (non-juvenile)
- Treatment of age-related macular degeneration
- Climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause*

etc…….

THE LANCET Oncology

2017, 18, 394

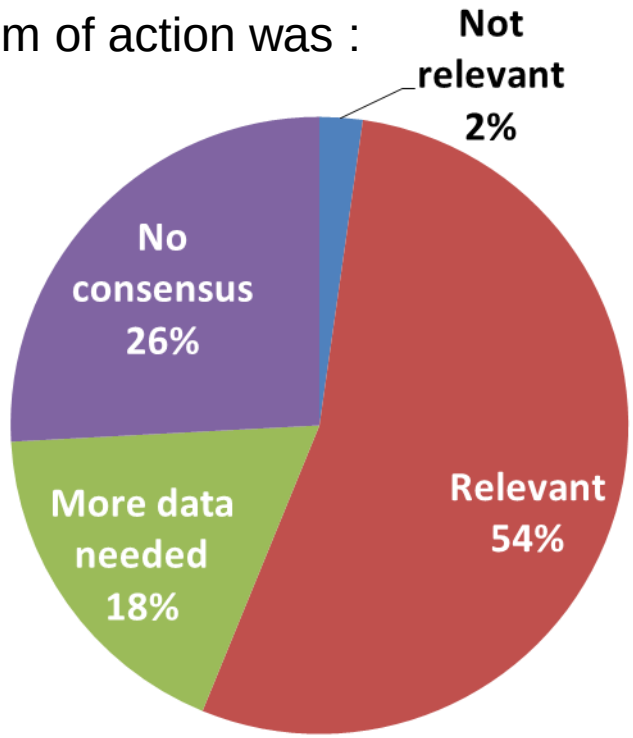
From class waivers to precision medicine in paediatric oncology

Andrew D J Pearson, Stefan M Pfister, Andre Baruchel, Jean-Pierre Bourquin, Michela Casanova, Louis Chesler, François Doz, Angelika Eggert, Birgit Geoerger, David T W Jones, Pamela R Kearns, Jan J Molenaar, Bruce Morland, Gudrun Schleiermacher, Johannes H Schulte, Josef Vormoor, Lynley V Marshall, C Michel Zwaan, Gilles Vassal, on behalf of the Executive and Biology Committees of the Innovative Therapies for Children with Cancer European Consortium*

2011-2015
147 class waivers
for 89 oncology drugs

Literature search
And 15 experts

Their mechanism of action was :



☞More biological and preclinical data are required to estimate the relevance of oncology drugs for pediatric malignancies

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PDCO reviewed most class waivers in July 2015

Previous class waiver: For all "medicinal products intended to treat lung carcinoma (small cell and non-small cell carcinoma)"

"The revised waivers are: [...]

the class of thymidylate synthase inhibitor medicinal products

Examples: Pemetrexed, Raltitrexed

for treatment of intestinal malignant neoplasms and lung malignant neoplasms;"

Conditions or groups of conditions

Warwick et al. Phase 2 Trial of Pemetrexed in Children and Adolescents [...] Pediatr Blood Cancer 2013, 60: 237
Malempati et al. Phase I trial and pharmacokinetic study of pemetrexed in children [...] J Clin Oncol 2007, 25: 1505
Horton et al. Phase I trial and pharmacokinetic study of raltitrexed in children [...] Clin Cancer Res 2005, 11: 1884

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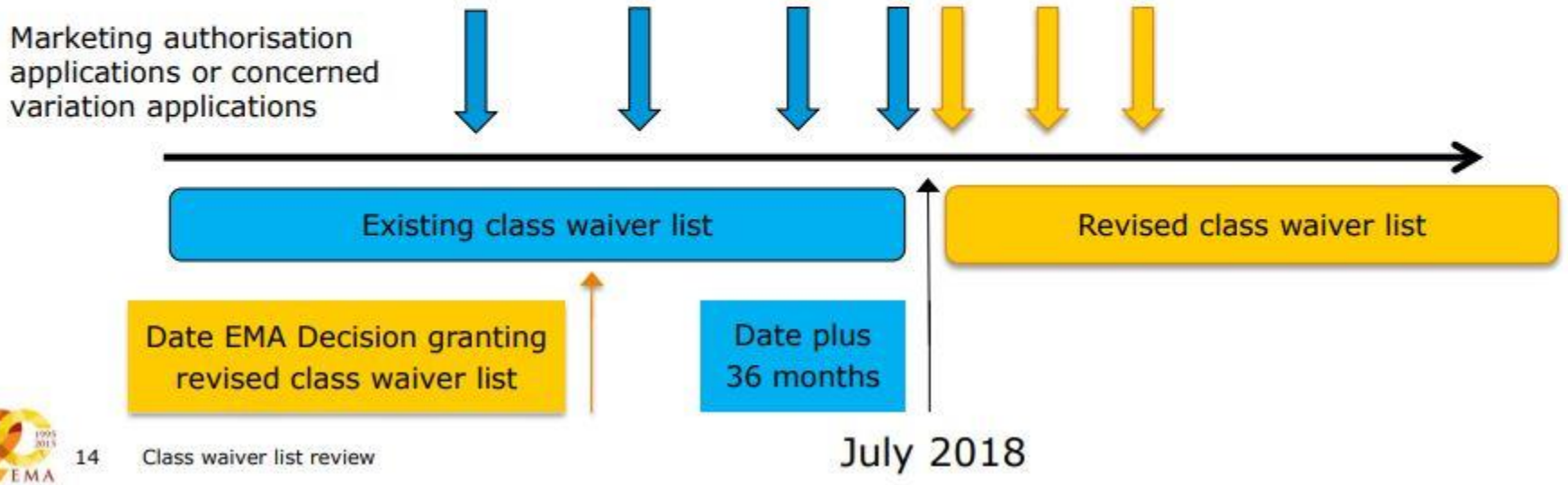
Transition period of 3 years

- Article 11 (3) Regulation (EC) No. 1901/2006: "If a particular product-specific or class waiver is revoked, the requirement set out in Articles 7 and 8 shall not apply for 36 months from the date of the removal from the list of waivers."



A specific waiver can still be granted to a medicinal product,
But the company needs to submit a dossier to justify the request

Improving cancer care for children and young people 3

New drugs for children and adolescents with cancer: the need for novel development pathways

Gilles Vassal, C Michel Zwaan, David Ashley, Marie Cecile Le Deley, Darren Hargrave, Patricia Blanc, Peter C Adamson

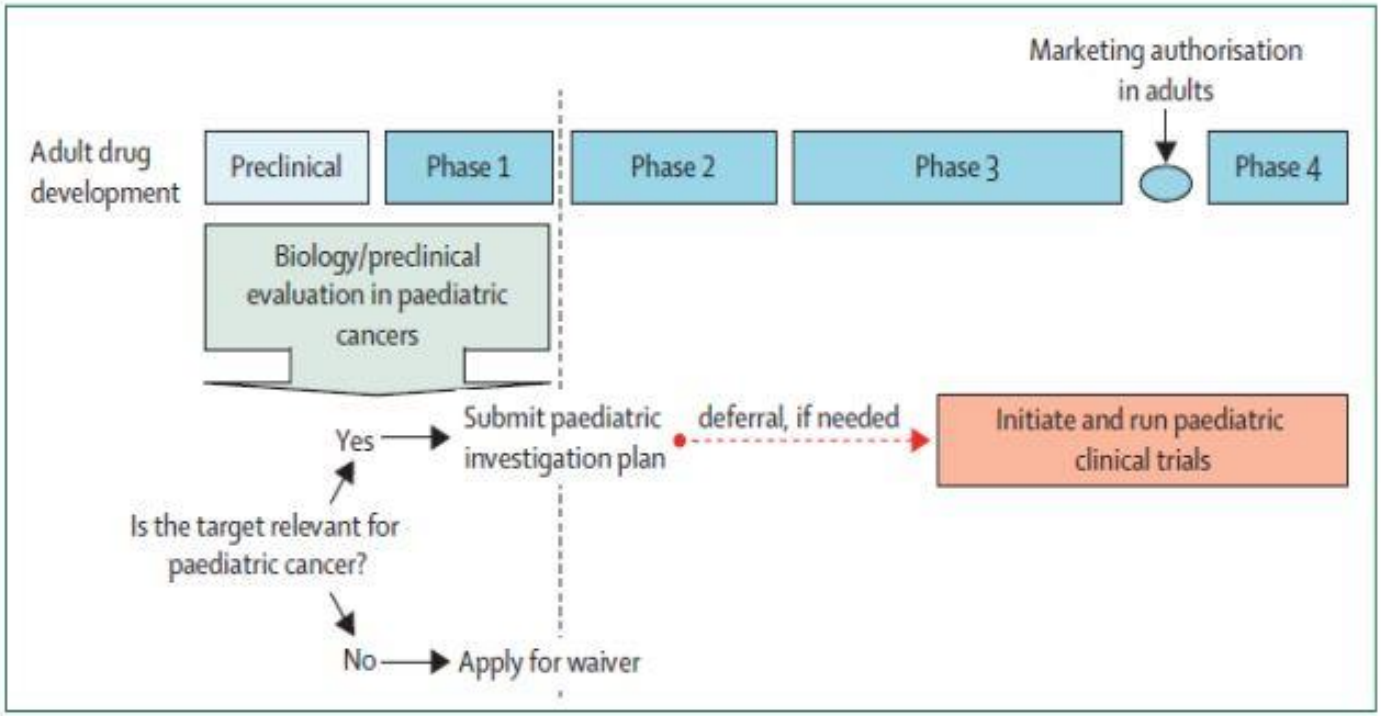


Figure 2: Proposed scheduling of an EU paediatric drug-development pathway

Class waiver list review

Vassal G et al. New drugs for children and adolescents with cancer: the need for novel development pathways. Lancet Oncology 2013, 14: e117

2018 and onward

New environment : RACE for Children and revised Class waiver list

CDDF - ITCC - SIOPE 4th Paediatric Oncology Conference

ACCELERATING THE DEVELOPMENT OF NEW ONCOLOGY DRUGS FOR CHILDREN AND ADOLESCENTS

20-21 January 2016
Brussels, Belgium

Proposals

1. Pediatric development should be based on drug **mechanism of action** instead of adult indication
2. **Prioritisation** should be set up to choose compounds to be evaluated or not in children
   - Based on MOA, needs, feasibility
   - Using stonger biological and preclinical data
   - Done through multistakeholder forum
3. **Reduce delay in starting pediatric development**
4. **New incentives and rewards**

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER