EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

“Significant Benefit” across provisions

STAMP – 3rd December 2018

Presented by EMA Regulatory Affairs Office

An agency of the European Union

Background

Has been part of the **work-plan** for CHMP, COMP, PDCO

Drafted with **Sponsors from the Committees** and support from EMA

Key objectives

• Understanding the different concepts and purposes of 'significant benefit' provisions (during analysis scope expanded also to other comparative assessments).

• Review how assessment of "significant benefit" is applied across different legislative provisions.

Scope

- 'significant clinical benefit' (for an additional year of marketing protection)

  Article 14(11) of Regulation (EC) No 726/2004)

- 'significant benefit' (for orphan designation)

  Article 3.1(b) of Regulation (EC) No 141/2000

- 'clinical superiority' (for derogation from orphan market exclusivity)

  Article 8(3) of Regulation (EC) No 141/2000

- 'significant therapeutic benefit' (for PIP waiver)

  Article 6(2) and 11.1(c) of Regulation (EC) No 1901/2006

- significant differences in efficacy and safety (for NAS)

  Article 10(2) of Directive 2001/83/EC

- 'major therapeutic advantage' (for a conditional marketing authorisation)

  Article 4 of Regulation (EC) No 507/2006

- 'major public health interest' (for accelerated assessment)

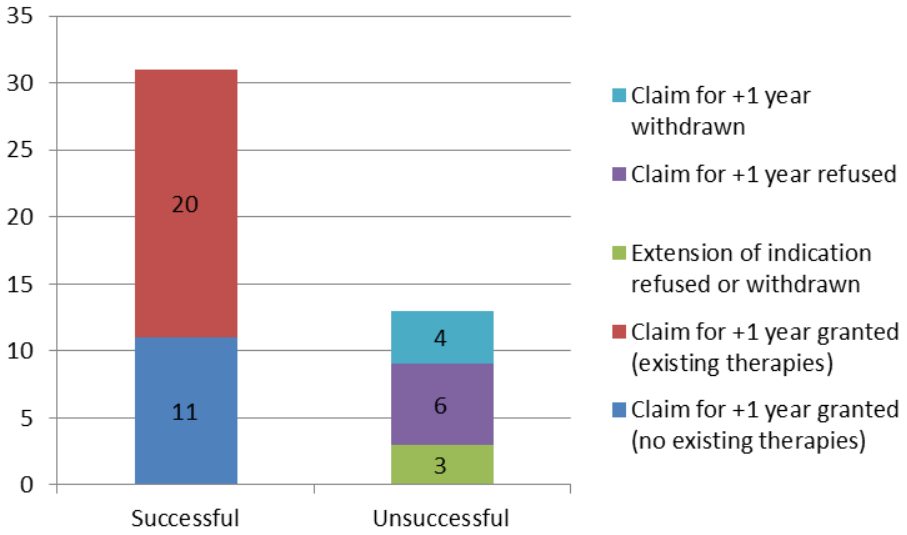
  Article 14(9) of Regulation (EC) No 726/2004

	+1 year marketing protection	Orphan designation (incl. maintenance)	Clinical superiority (Orphan derogation)	(Lack of) Significant therapeutic benefit for PIP waiver	New active substance status	Conditional marketing authorisation	Accelerated assessment
Key terminology	Significant clinical benefit	Significant benefit	Clinical superiority	Significant therapeutic benefit	Significant differences in safety and/or efficacy	Unmet medical needs, Major therapeutic advantage	Major public health interest, therapeutic innovation, unmet medical needs
Legislation	Art 14(11) Regulation (EC) 726/2004	Regulation (EC) 141/2000 Art 3(2) Art 3(1)(b) Regulation (EC) 847/2000	Art 8, Regulation EC (No) 141/2000 –Market exclusivity Art 3, Regulation (EC) No 847/2000	Art. 7(1), 6(2) & 11(1)(C) Regulation (EC) 1901/2006	Art 10, Directive 2001/83/EC Annex I, Part II, 3. of Directive 2001/83/EC	Art 13(7) Regulation (EC) 726/2004 Art 4(1)(c) EC Regulation 507/2006 Art 4(2) Regulation 507/2006	Art. 14(9), Regulation (EC) No 726/2004
Guidance	Guidance EC November 2007	Commission notice (2016/C 424/03)	EC Communication (C(2008) 4077 final)	EC Communication (2014/C 338/01)	Reflection paper (EMA/651649/2010)	Guideline EMA/CHMP/509951/2006 Rev 1	Guideline EMA/CHMP/671361/2015 Rev. 1
Who assesses?	**CHMP**	**COMP**	**CHMP**	**PDCO**	**CHMP**	**CHMP**	**CHMP**
Benefit	+1 year marketing protection (8+2**+1**)	10-year orphan market exclusivity and other incentives	Breaking orphan market exclusivity of another product	PIP Waiver	New active substance status	Conditional MA	Shortened assessment timelines
Time of assessment	After completion of respective development	Early in development + confirmation at time of granting MA	After completion of respective development	Early in development (by the time of completion of adult PK studies)	After completion of respective development	After partial completion of respective development (some confirmatory studies pending/due)	Shortly prior submission of the MA application

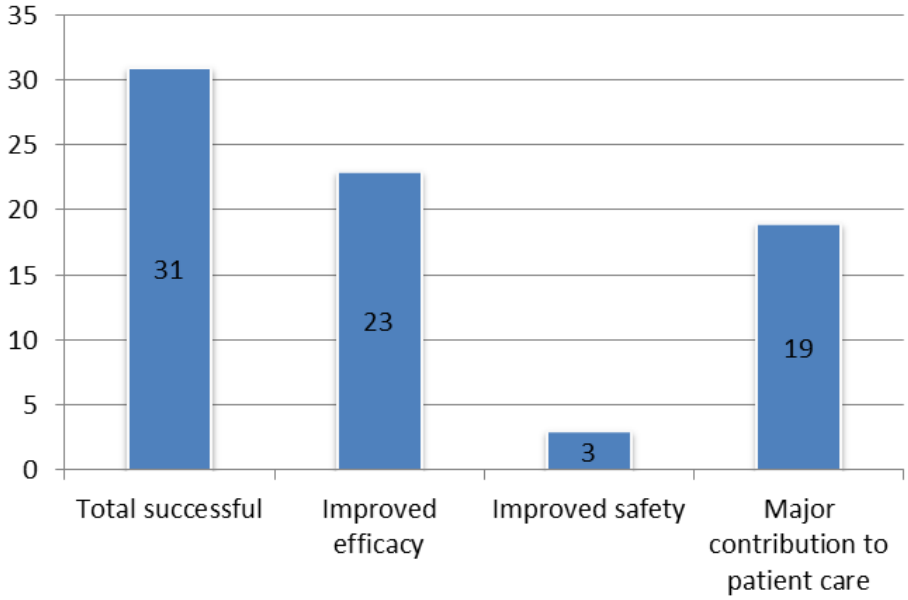
Example of a summary of experience

+1 year of marketing protection

Overview of claims received



Grounds for accepting the claims



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Example of a summary of experience

Categories of grounds for paediatric waivers

- Numerous and/or better treatment alternatives already available;
- Data in paediatric population available;
- Available data can be extrapolated;
- Demonstration of significant therapeutic benefit/ conduct of meaningful studies not feasible;
- Available data does not indicate that significant therapeutic benefit is likely;
- The new route of administration being developed is not deemed to be needed or to bring an incremental benefit for the paediatric population;
- No unmet paediatric need identified;
- Favourable natural history does not warrant invasive therapy;
- Others (e.g. fixed dose combination vs. individual monocomponent products).

Observations and conclusions

3 key elements:

1) (improved) efficacy,
2) (improved) safety or
3) major contribution to patient care

Not at the expense of **overall B/R balance**

Direct comparative clinical data preferred.

Onus on the applicant, but committees to consider if important elements have not been omitted.

Provisions differ in their nature.

Any questions?

Further information

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