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Harmonisation of the assessment of Multinational Clinical Trials

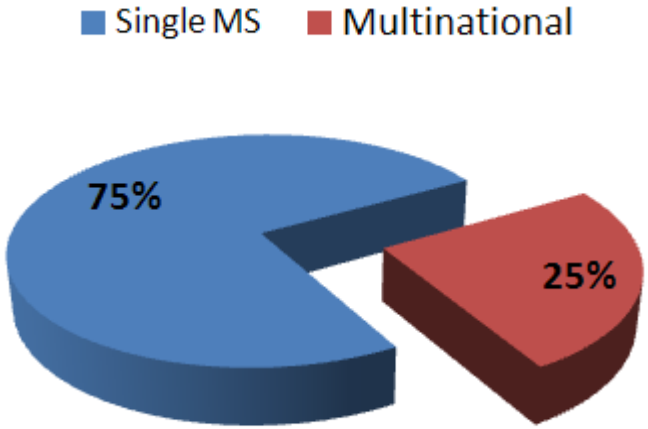
Making gene and cell therapy medicines a reality

Gibson Hotel, Dublin. 11th July 2012

Dr. Agnieszka Przybyszewska, MD, PhD

Clinical trials in the EU

In the EU approx. 4,000-6,000 clinical trials are performed each year. This equals approx. 8,000 – 10,000 clinical trial applications.



This equals approx. 60% of all clinical trial applications, and to approx. 70% of all trial subjects.

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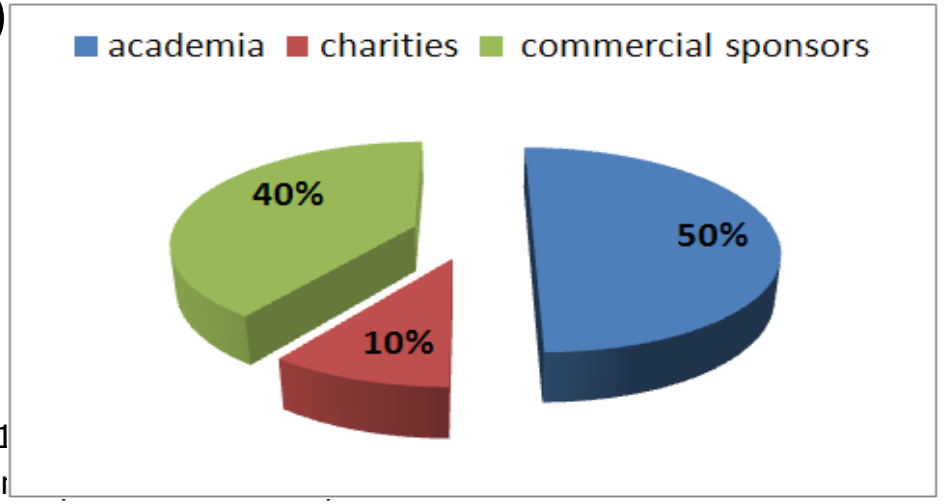
Source: DG Sanco (2011), Concept Paper Submitted For Public Consultation

Clinical trials in the EU- ATMP

The majority of trials conducted in single-member state (the sponsor was also based in the state in question)



Source: Mol Ther. 2012 Mar;20(3):479-82. doi: 1
Clinical development of advanced therapy medici
regulators must be proactive. Maciulaitis R, D'Apote L, Buchanan A, Pioppo L, Schneider CK.

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European Clinical Trials Directive 2001/20/EC

Established to:

- provide greater protection to subjects participating in clinical trials
- ensure quality of conduct
- harmonise regulation and conduct of clinical trials throughout Europe

Clinical Trials Directive=
achievements but also **shortcomings**

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European Clinical Trials Directive 2001/20/EC

- Implementation of Directive

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Situation after the implementation of the Clinical Trials Directive

Impact on Clinical Research of European Legislation "ICREL" study

Differences between 2003 (i.e. prior to the entry into force of the CT Directive) compared to 2007

In general no decrease in clinical research activity in the EU.

However,

- Performing clinical trials has become more difficult and costly

Source:http://www.efgcp.be/icrel/

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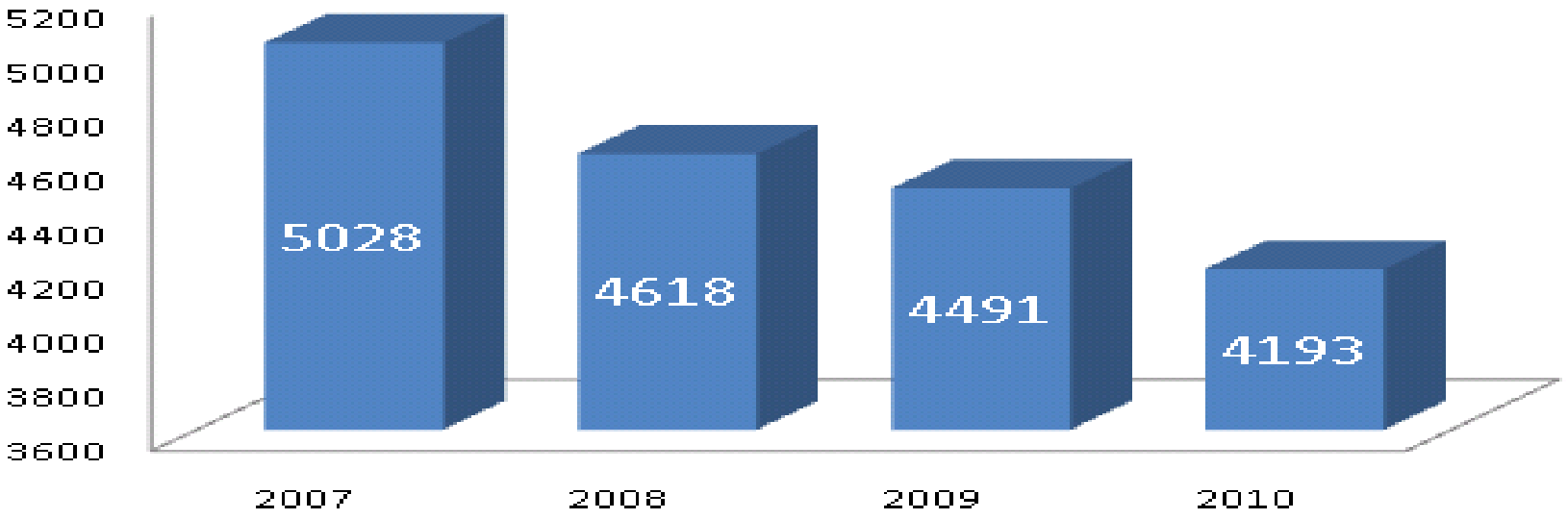
Situation after the implementation of the Clinical Trials Directive

Number of clinical trials applied for in the EU



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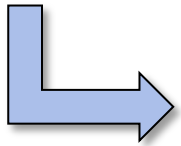
Source: DG Sanco (2011), Concept Paper Submitted For Public Consultation

Clinical trials in the EU

- Multiple and divergent assessments of clinical trials (fragmentation of the authorisation regime)

  - Multinational Clinical Trial Applications **(CTA)** are assessed by several National Competent Authorities **(CA)** independently

  - In each MS CTAs are assessed by NCAs and Ethics Committees independently



Divergent decisions (approvals/conditional approvals/refusals) may be reached for the same clinical trial by different MS

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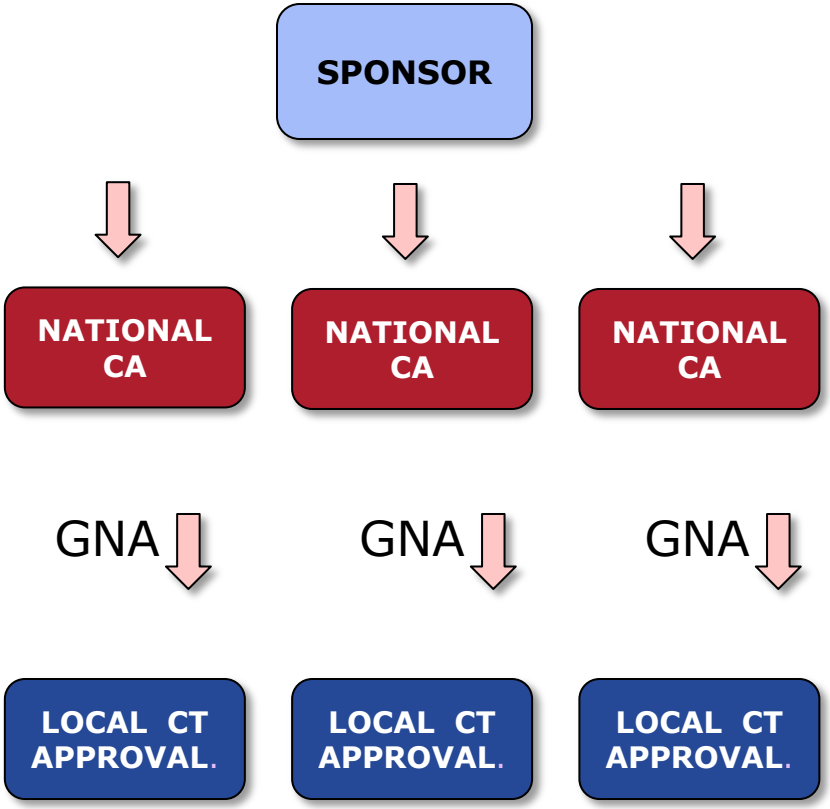
Clinical trials in the EU



Questions from CAs requiring individual responses from sponsor

Divergent decisions (approvals/refusals conditional approvals)

GNA=Grounds for non-acceptance

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Clinical trials in the EU – other national bodies

Ethics Committees
Independent assessment

In most the EU countries **the environmental risk assessment** is performed by the another national body

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Clinical Trials Facilitation Group (CTFG)

- Established by Heads of Medicines Agencies (HMA)
- Representation: 27 national Competent Authorities, European Commission and European Medicines Agency
- **Harmonizing processes** and practices relating to clinical trials mainly in the fields of clinical trial applications, clinical trial amendments and safety procedures
- **Developing data sharing** and participating in the improvement of information systems
- Developing communication with stakeholders and co-operating with other EU working groups
- Sharing of scientific assessment of multinational clinical trials – **Voluntary harmonization procedure (VHP)**

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Voluntary Harmonisation Procedure (VHP)

- **Co-ordinated assessment** of a clinical trial that is to take place in several European countries
- **Competent authorities only** not ethics committees
- Further information: www.hma.eu

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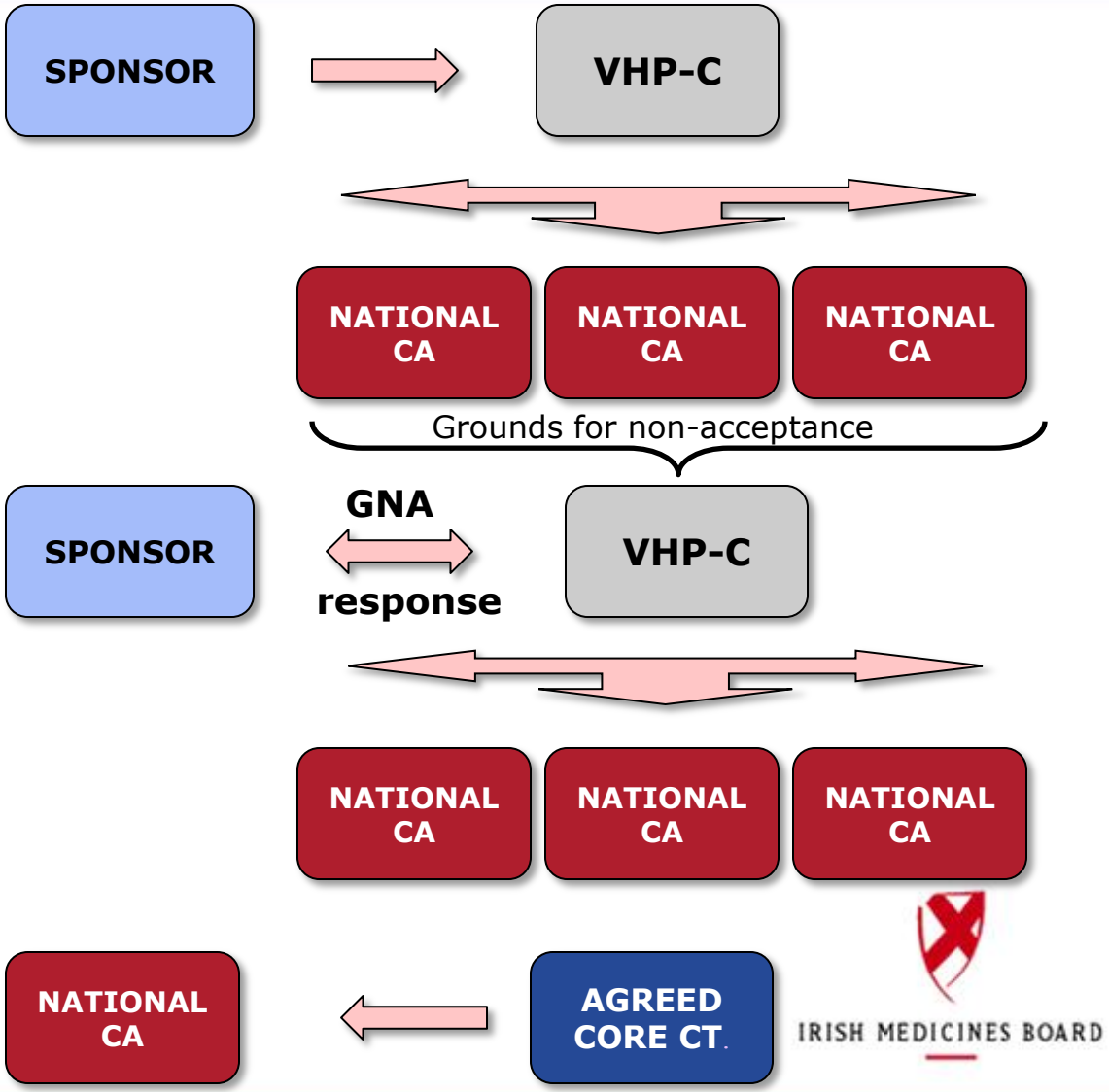
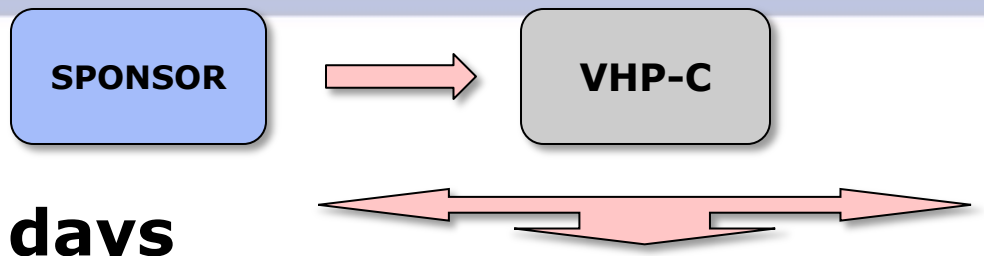
Voluntary harmonisation procedure



Voluntary harmonisation procedure



VHP-Phase 1: Request for VHP

- Request by sponsor sent to VHP coordinator **(VHP-C)** including the identification of the participating NCAs and submission of a full dossier

- Decision by Member States to participate in the VHP **(Voluntary procedure- some MSs do not participate)**

- **Reference** National Competent Authority is selected

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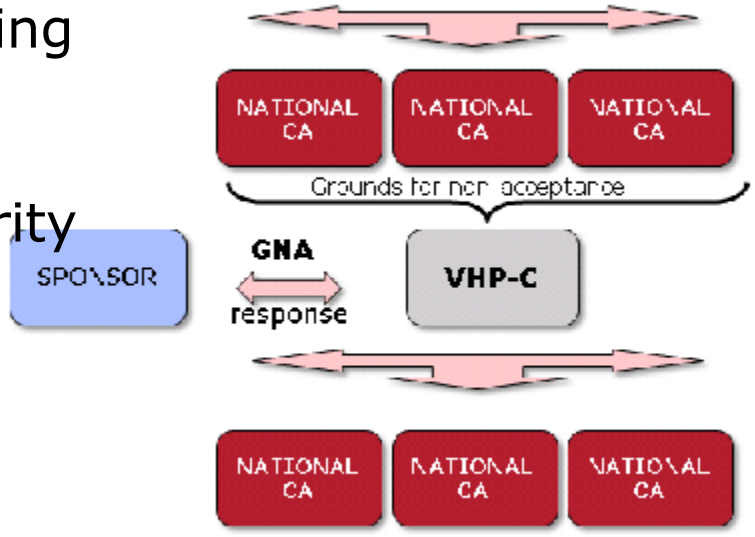
Voluntary harmonisation procedure

VHP-Phase 2: Assessment

- Review of the CTA by all the participating NCAs
- **Reference** National Competent Authority is leading assessment
- **One harmonized list of question**
- Common position agreed at the end of the procedure
- Administrative co-ordination by the VHP coordinator



Max. 60 days

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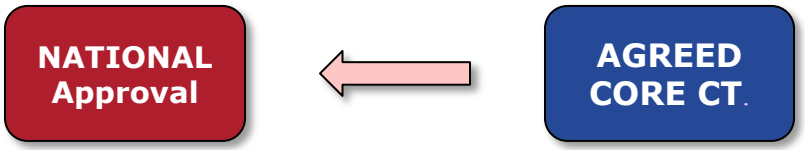
Voluntary harmonisation procedure

VHP-Phase 3: national Member States step

Formal CTA applications to NCAs.
CTA approval by NCAs within short timelines (after positive VHP)

10 days



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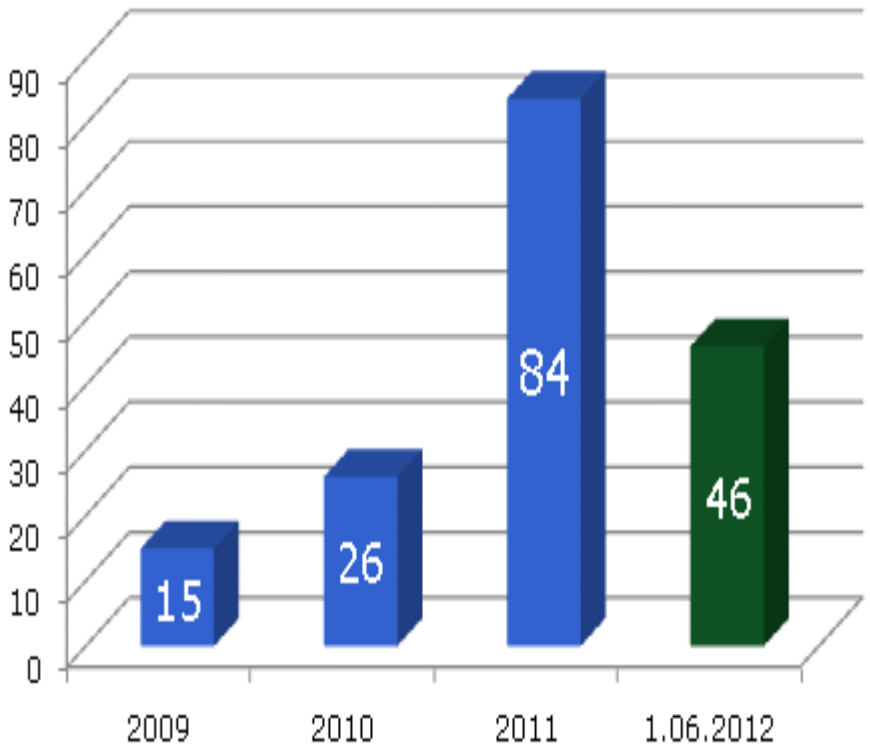
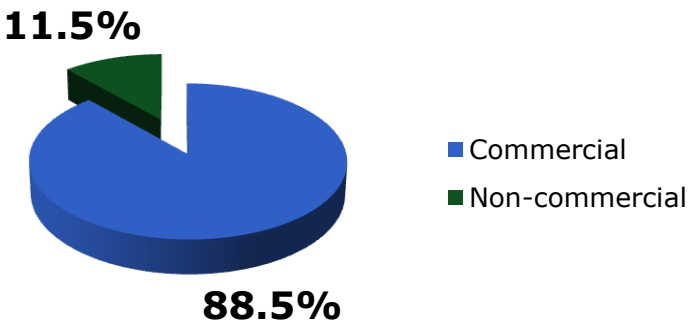
Voluntary harmonisation procedure

Number of VHPs per submission year





Source: The Heads of Medicines Agencies- http://www.hma.eu/77.html

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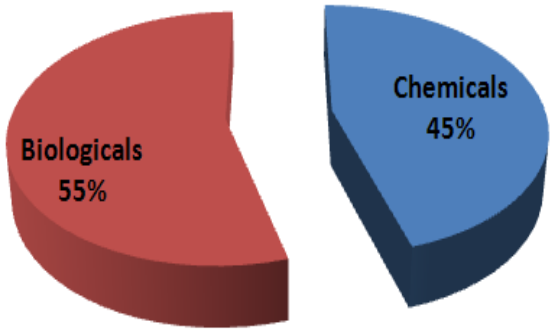
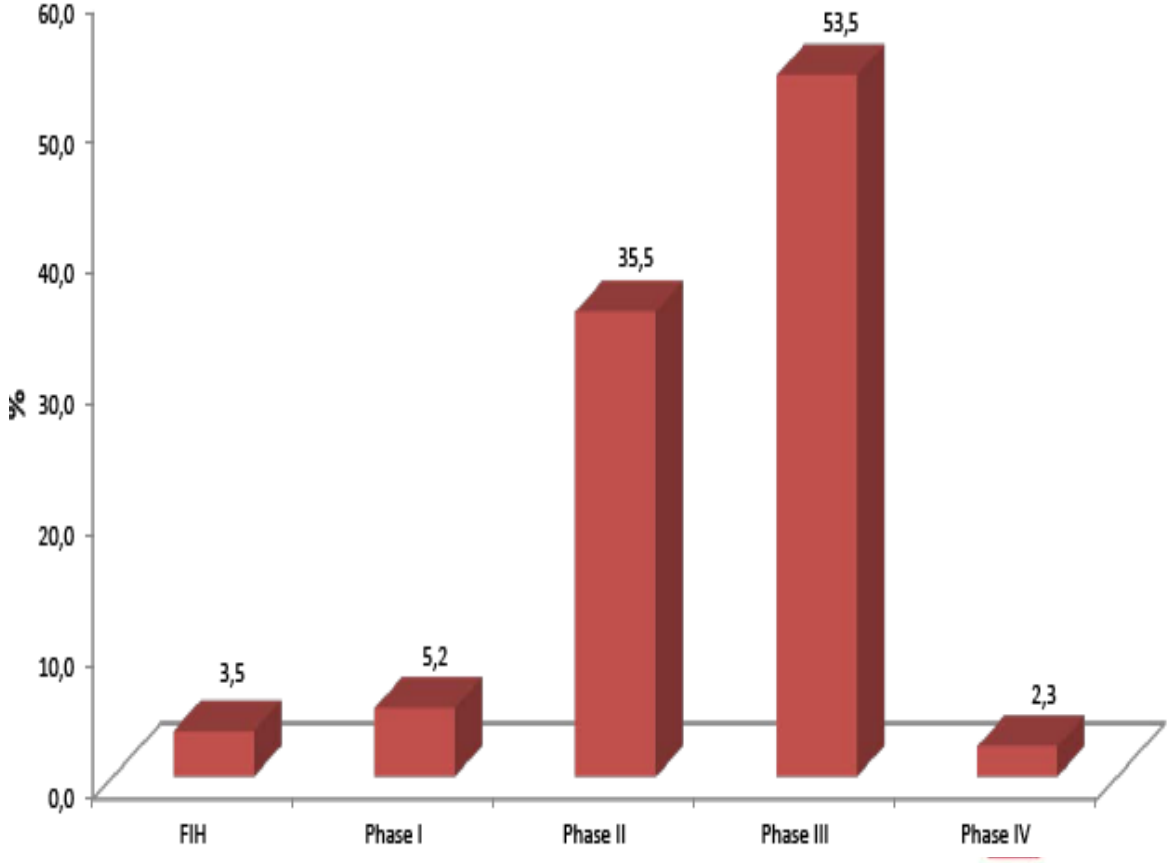
Voluntary harmonisation procedure

Distribution of the IMPs

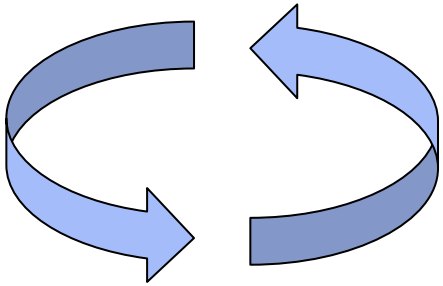


Distribution of the VHPs by phase



Voluntary harmonisation procedure

- Voluntary harmonisation procedure allows for exchanging information/experience between the participating MSs (important for ATMP clinical trials)



Reduction of Ground for non-Acceptance (GNA)

The number of GNA per VHP is reduced by more than 50% in comparison to the GNA of the individual National Competent Authorities.

Source: The Heads of Medicines Agencies- http://www.hma.eu/77.html

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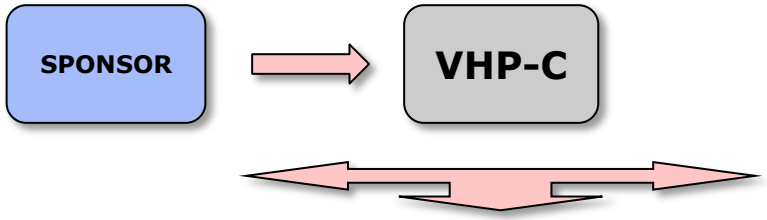
Voluntary harmonisation procedure for ATMPs

ATMPs clinical trials have been accepted for Voluntary Harmonisation procedure



Recently 3 ATMP-CTs have been assessed through VHP

Note:

Gene therapy CTs - with some flexibility and depending on the concerned MS

(many countries have bodies outside the NCAs that might have to be involved)

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Revision of the Clinical Trials Directive 2001/20/EC

The Clinical Trials Directive 2001/20/EC will be replaced by the Clinical Trials Regulation.

- Implementation of Directive

- Implementation of Regulation

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Revision of the "Clinical Trials Directive 2001/20/EC

Expected changes as per "concept paper":

- single submission portal
- coordinated assessment procedure (CAP)

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Any questions?

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