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Clinical trials legislation – focus on radiotherapeutics

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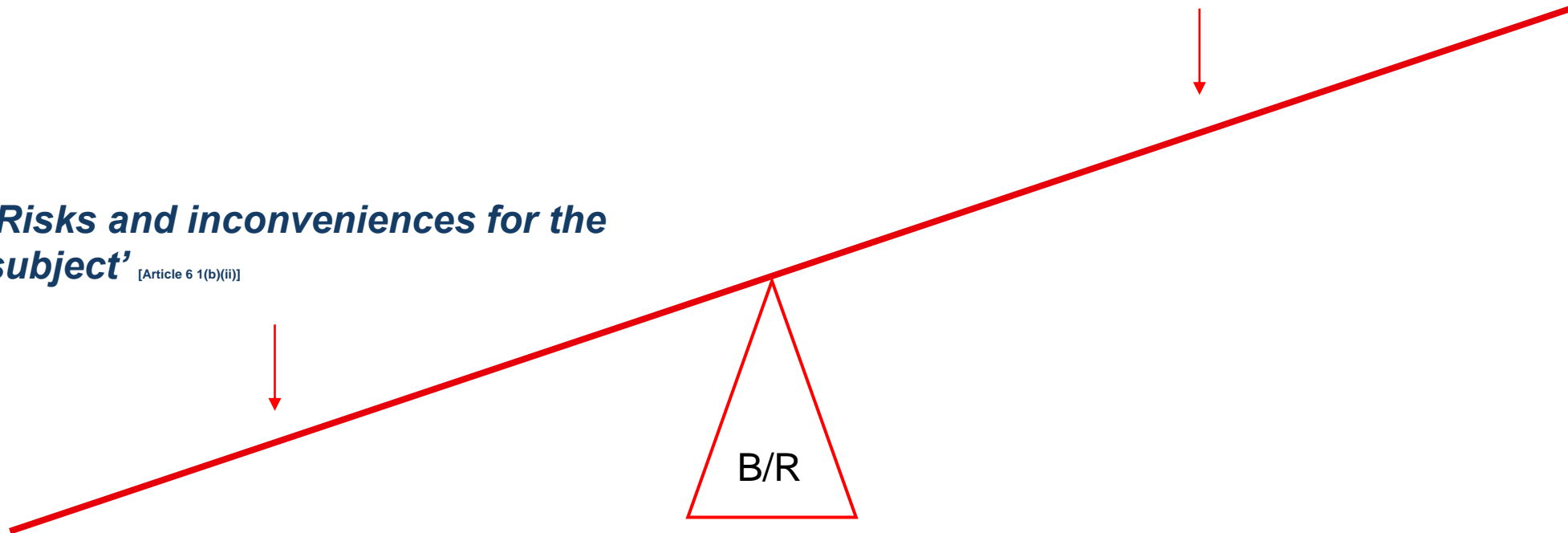
Regulation (EU) No 536/2014 – Clinical Trials

- Applies since January 2022 (adopted May 2014)
 - Single decision per Member State (National Competent Authority & Ethics Committee)
 - Clinical trials are interventional clinical studies – protocol steers therapeutic choice and/or subject monitoring = clinical studies outside normal clinical practice
- 1. Ensures patient safety & scientific data robust and reliable
- 2. Harmonises approval process – common review of multinational applications
- 3. Streamlines submission and review process via EU Portal and Database (Clinical Trials Information System) – strict timelines - tacit approval
- 4. Increases transparency compared to earlier legislation

Benefit-risk balance – bases for assessment & decision on trial applications

'Anticipated therapeutic and public health benefits' [Article 6 1(b)(i)]

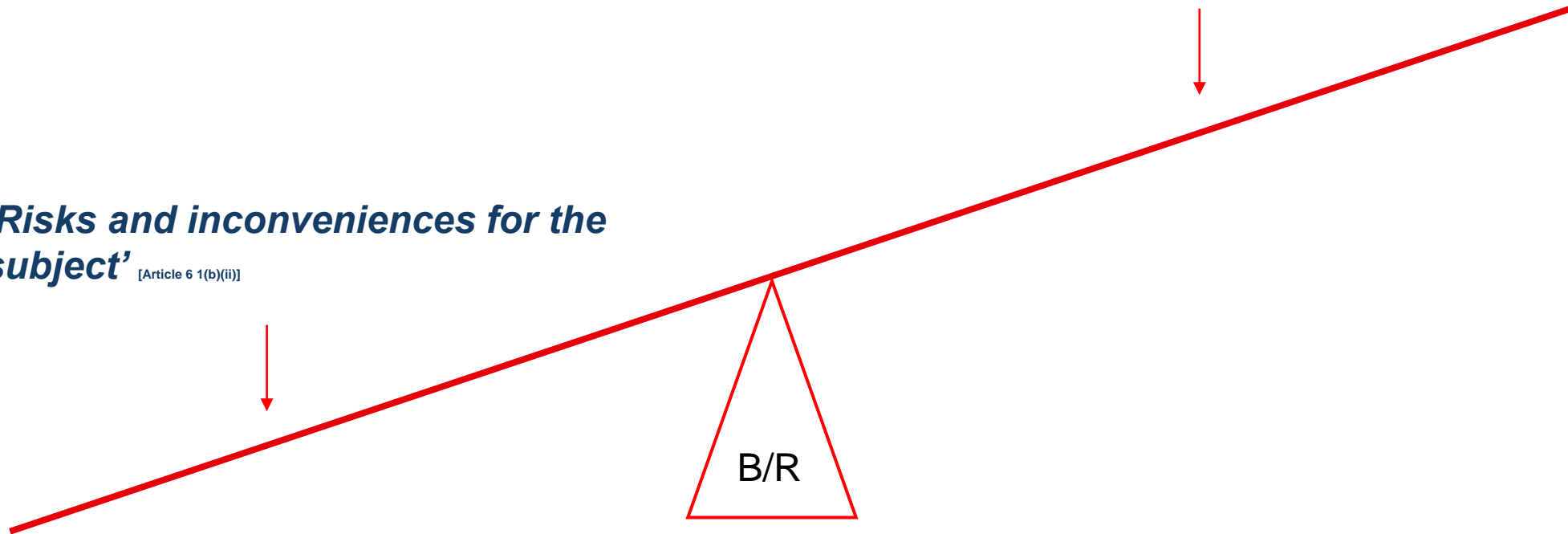
'Risks and inconveniences for the subject' [Article 6 1(b)(ii)]



Benefit-risk balance – bases for assessment & decision on trial applications

*‘Anticipated **therapeutic and public health benefits**’* [Article 6 1(b)(i)]

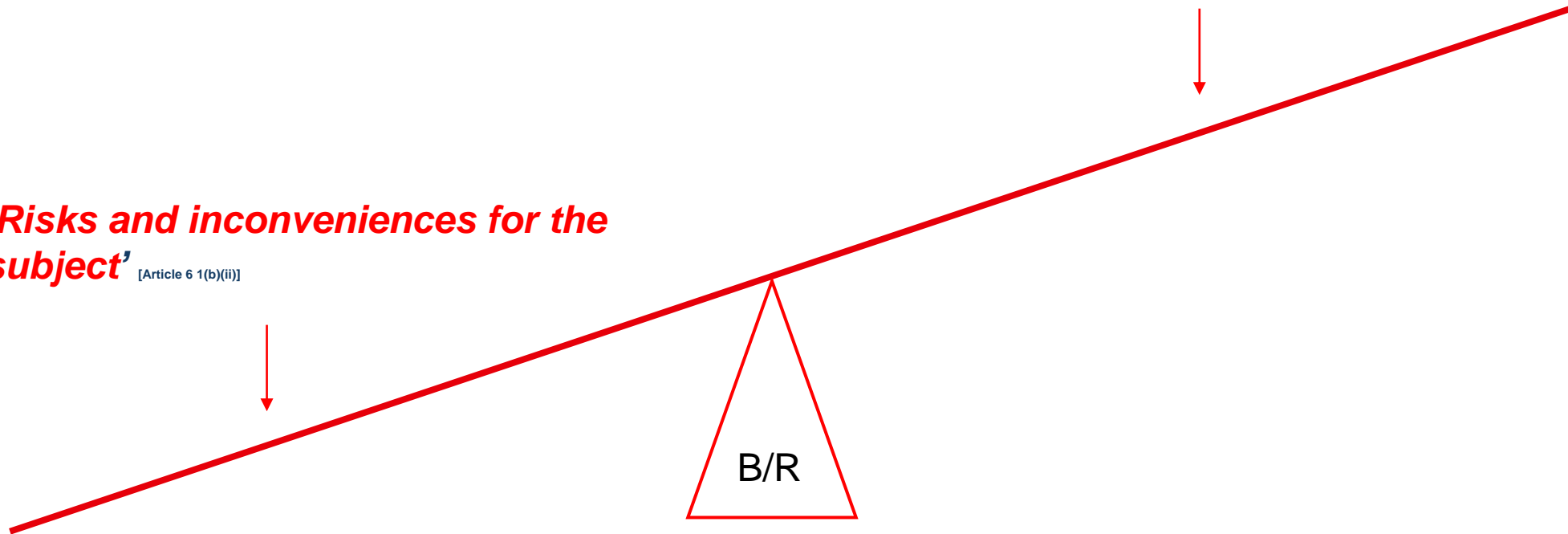
‘Risks and inconveniences for the subject’ [Article 6 1(b)(ii)]



Benefit-risk balance – bases for assessment & decision on trial applications

*‘Anticipated **therapeutic and public health benefits**’* [Article 6 1(b)(i)]

*‘Risks and inconveniences for the **subject**’* [Article 6 1(b)(ii)]



Radiotherapeutics - Questions and Answers on CTR, Eudralex vol 10 (Question 7.51, 408)

Radiotherapeutics in clinical trials - systemic radiation therapies with radiopharmaceuticals

AHASA – target absorbed radiation dose *as high as safely attainable* preventing severe and/or irreversible long-term toxicity while at the same time maintaining a high likelihood of efficacy

Protocol benefit/risk - ***dosimetric procedures absorbed doses (Gy) to target tumour lesions and dose limits to risk organs*** based on best available evidence, necessary adaptations of treatment plan due to combination therapy interfering with biological effect of radiation therapy

CTAG meeting 27 Nov 2023

Chaired by European Commission DG SANTE

Decided to set up a subgroup on radiotherapeutics

Aim: clarity and harmonise requirements for trial sponsors

- Although **dosimetry** has been used in clinical trials on a voluntary basis for many years, there is **no accepted international standard**. Basic standards for dosimetric procedures used in clinical trials therefore need to be further clarified
- If **firm evidence is lacking** on e.g. target tumour dose and/or dose limits to risk organs for certain isotope or indication, sponsor should consider including **endpoints** on analysis of **dose vs response for efficacy and/or toxicity**
- In situations where **target lesions not identifiable** (e.g. adjuvant treatment of micrometastases), treatment should be **planned primarily with respect to risk organs**

DG SANTE will invite DG ENERGY experts on the Euratom Directive (2013/59)

Thanks for your attention
Questions welcome!

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Back-up slide on radiodiagnostics

Radiodiagnostics - Questions and Answers on CTR, Eudralex vol 10 (Question 7.51, 408)

Radiological procedures, nuclear medicine procedures

ALARA – radiation exposure *as low as reasonably achievable* without compromising diagnostic imaging quality

Risks and inconveniences radiation exposure described in protocol, justified in comparison to normal clinical practice

Risk category trial participants ICRP criteria, radiodiagnostic trial procedures, maximum effective dose per procedure (mSv), number of procedures/trial participant/year, and estimated number of additional radiodiagnostic procedures/trial participant/year compared to normal clinical practice for the same indication