AUTORITÀ GARANTE DELLA CONCORRENZA E DEL MERCATO
AGCM

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Facultad de Derecho

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Exploitative conducts in the pharmaceutical sector: from the Aspen case to the new frontiers of innovative/orphan drugs

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Usual disclaimers apply

«DRUGSPLOITATION»: RECENT NEWS

MAY 24, 2019

FDA approves $2M r… ever

by Linda A. Johnson

This photo provided by Novartis shows …

U.S. regulators have approved the m… that destroys a baby's muscle contro… common type of the disease within …

FAIR PR… JOHA…

11

World Health Organization

SEVENTY-SECOND WORLD HEA…
Agenda item 11.7

Improving the … medicines, vacci…

Draft resolution propo… Greece, India, Italy, Keny… Russian Federat… Spa…

The Seventy-second World Hea…

PP1 Having considered the Report b… its annex "Draft Road Map for access … by the Director-General on Medicine… EB144/18), pursuant to resolution WH…

PP2 Recognizing the critical role pl… in bringing new treatments and value …

FOOTNOTE: For the purposes of this … devices, diagnostics, assistive product…

PP3 Recognizing that improving a… requires action at, and adequate know… development to quality assurance, regu…

PP4 Seriously concerned about the … within and among Member States as … impede progress towards achieving Universal Health Coverage;

Press release

3 drug firms accused of illegal market sharing

The CMA has provisionally found that 3 drug firms signed an illegal agreement that resulted in significant price hikes for an essential medicine.

Published 3 October 2019
From: Competition and Markets Authority

In a Statement of Objections to be issued today, the Competition and Markets Authority (CMA) sets out its provisional view that, in 2016, pharmaceutical company Aspen unlawfully agreed to pay 2 other firms, Amilco and Tiofarma, to stay out of the UK market for fludrocortisone acetate tablets. This is a prescription-only medicine that thousands of patients rely on to treat primary or secondary adrenal insufficiency, commonly known as Addison's Disease.

«DRUGSPLOITATION»: RECENT CASE-LAW

- Exploitative abuses in the pharmaceutical markets are raising increasing attentions by antitrust enforcers.

- Notwithstanding many technical difficulties of excessive pricing cases – information asymmetries about product's cost structures, interplay with complex sectoral regulations and different pricing policies at national levels – it is quite certain that an antitrust focus will be kept on the pharma sector, first of all because its socio-economic relevance.

- Recent cases managed by EU national competition authorities proved to be valuable for better defining applicable legitimacy tests – and checking their judicial affordability.

  - Italy: ICA's proceedings A480 («Aspen case»). The decision was issued on September 2016 and it has been upheld by the First Instance Administrative Tribunal (TAR) on October 2017, final appeal is pending.

    - Please note: a EU-wide investigation on the same Aspen's conducts has been launched by the EU Commission on May 2017, and is currently ongoing.

  - UK: Pfizer/Flynn case (CMA decision issued on December 2016, quashed by the Competition Appeal Tribunal on June 2018; revision pending).

THE ASPEN CASE: A SHORT INTRODUCTION

- On 19 November 2014 ICA opened an investigation against South-African based Aspen Group in order to verify a possible infringement of art. 102 TFEU.

- The investigation focused on price increases that Aspen requested and obtained by the Italian medicines authority («AIFA») for a product portfolio of old antineoplastic drugs (Alkeran, Leukeran, Purinethol, and Tioguanine) previously bought from GSK in 2009.
  - off-patent drugs, used for treating severe blood cancers
  - prices entirely reimbursed by the NHS (so-called «class A» drugs)
  - prices valid in 2013 weren't updated since decades

- In march 2014 Aspen, AIFA recognized substantial price increases, then filed a complaint to ICA:

Product name	Active ingredient	% increase in price
Alkeran	melphalan	+1540%
Alkeran inj	melphalan	+257%
Leukeran	chlorambucile	+1166%
Purinethol	mercaptopurine	+465%
Tioguanina	tioguanina	+306%

- On 29 September 2016 ICA fined Aspen for the infringement of Article 102, lett. a), TFEU for unfair pricing obtained by misusing its right to renegotiate prices with AIFA.

THE ASPEN CASE: A SHORT INTRODUCTION

- As for the market definition and dominant position, ICA: *(1)* defined four product markets at ATC5 level; *(2)* assessed the lack of any possible alternative for consumers.
- As for the conducts, Aspen was considered plainly aggressive against AIFA, that had no countervailing power.
  - AIFA was bound to keep the drugs on the Italian market and reimbursed by the NHS (please note: because of a law adopted in 2012, even without a pricing agreement drugs can be sold, but with full costs borne by the patients).
- ICA considered case-specific elements to evaluate the general unfairness of prices applied by Aspen, such as:
  - a comparison in itself between ex ante and ex post prices (price spikes ranging from +300% to +1500%);
  - absence of any economic justifications for so relevant increase (no R&D costs whatsoever);
  - absence of any non-cost related factor leading to an improvement in quality or in the level of service offered to the NHS or patients.

THE ASPEN CASE : A SHORT INTRODUCTION

- Remember: when dealing with excessive pricing, a two-stage unfair price test has been established within the EU antitrust since the United Brands case (1978).
  - first stage: difference between costs and prices is excessive;
  - second stage: price is unfair either in itself or compared to competing products:
    - price has no reasonable relationship with «economic value»
      - cost and non-cost related factors (see the Helsinborg case, 2004)
      - + reasonable profit margin
    - comparison with the prices set
      - for the same product in different geographical markets
      - for competing products
- As for the burden of proof, see the AKKA/LAP case (2017)
  - Competition authorities must show that difference is significant and persistent;
  - it is for dominant undertakings to show that price is fair based on objective factors.

THE ASPEN CASE : A SHORT INTRODUCTION

- ICA developed its analysis by using two different considerations of possible excessive prices.
- In line with the United Brands test, ICA verified Aspen's pricing conducts by considering:
  - a measure of the excess of prices on the economic value of the drugs;
  - other factors pointing towards the unfairness of prices imposed by Aspen.
- First of all, ICA focused on Aspen's gross margin, *i.e.* it calculated the difference between *ex ante* prices and direct costs borne by the company; the resulting gross margin in % of sales was then compared to the total indirect costs in % of sales.
- On the basis of that, ICA concluded that:
  - prices before the requested increase already granted a margin in line with Aspen's average margins;
  - as a consequence, price spikes ranging between 250% and 1500% were excessive *vis-à-vis* the product's economic value.

THE ASPEN CASE : A SHORT INTRODUCTION

- The ICA also calculated the difference between prices and a comprehensive measure of costs – called «cost plus» - including direct costs + an apportionement of indirect costs + a reasonable rate of Return On Sales («ROS»).
- The analysis allowed to conclude that prices applied by Aspen:
  - generated excess in % of cost plus ranging from 100% to almost 400%
  - such percentages were well above those considered abusive in previous case-law (*e.g.*, Deutsche Post: 25%; Albion Water II: 46%)
- The excess ranges from round 100% to almost 400%, depending on assumptions on the rate of return granted in the calculation (13%, the average ROS of the sector, or 18%, the specific Aspen group ROS) and the inclusion of the trademarks purchase:
  - ROS 13% → excess between 145% and 374%
  - ROS 13% + trademarks → excess between 107% and 316%
  - ROS 18% → excess between 112% and 277%
  - ROS 18% + trademarks → excess between 83% and 240%

DRUGS AND EXCESSIVE PRICING: NEW FRONTIERS

- Please note: the Aspen case, as well as all the existing case-law related to drugs and excessive pricing, refers to mature products, where no innovation costs – as well as the need to protect incentives to pharmaceutical innovation – were at stake.
- In fact, antitrust authorities have been cautious when considering innovative drugs for fear of impairing further innovation: however, it seems that times are changing.
  - «[…] *high profits may be justified by risk taking or past investment, or the result of a firm's innovativeness and own excellence. The incentive for such efforts should not be undermined by ex-post competition law enforcement, because this could harm the dynamic competitive process and could reduce both innovation and consumer welfare. Where this is the case, pricing may not be unfair and enforcement not warranted. This does not mean, however, that Article 102(a) TFEU cannot be applied to abusive practices in the context of innovative products and risk-taking. […] competition authorities have to factor investments and innovation into their assessment of unfairness and need to be mindful of the effect of an intervention on dynamic efficiency.*»
    (130th OECD Competition Committee Meeting on 27-28 November 2018, *Excessive Pricing in Pharmaceutical Markets - Note by the European Union*, https://one.oecd.org/document/DAF/COMP/WD(2018)112/en/pdf)
- A highly significant test-bed for a new antitrust *interventionism* might be the Orphan Drugs («ODs») sector.

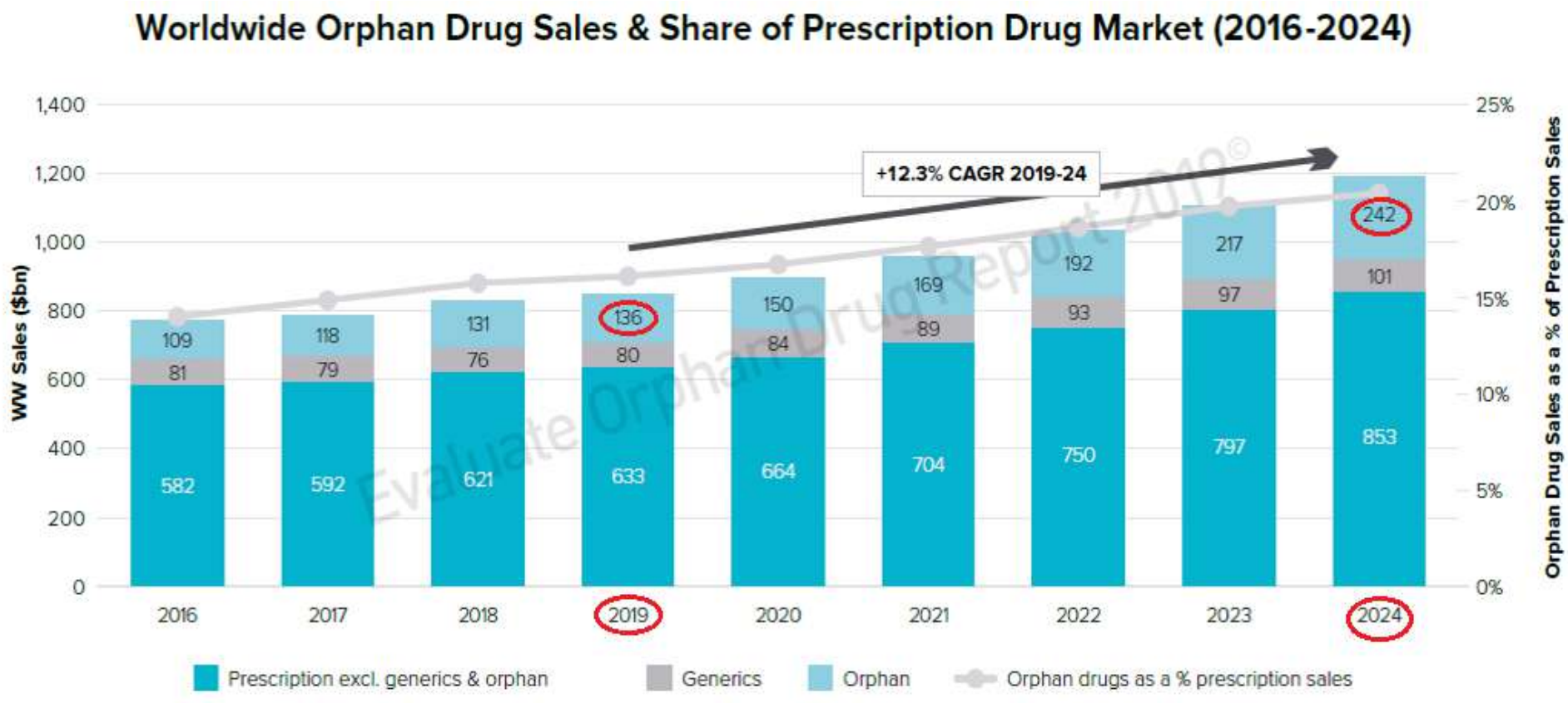
THE ORPHAN DRUGS SCENARIO

- ODs are medicines aimed to treat rare diseases
  - Historically, pharma companies have been reluctant to fund R&D for ODs: because rare diseases affect few people, profitability was deemed to be low.
  - In order to solve the issue, a growing number of incentive legislations has been enacted (USA, 1983; Australia, 1990-1997; Japan, 1993; EU, 2000).
- According to EU Regulation no. 141/2000, ODs are intended to treat:
  - a condition concerning no more than 1 in 10,000 people in the EU; or
  - a condition unlikely to offer sufficient economic incentives with reference to the initial investment, and
  - no authorized method of treatment already exist for that condition. If such method exists, the medicinal product concerned must have a significant impact on patient.
- Following EU provisions, ODs are granted – through centralized procedure managed by the European Medicines Agency – with a 10-year market exclusivity, during which the EU and the Member States cannot accept new marketing requests for drugs treating the same condition.
  - Please note: EMA can reduce market exclusivity period to 6 years, if product proves to be sufficiently lucrative.

THE ORPHAN DRUGS SCENARIO

- Incentives provoked a booming development of ODs (more than 450 approved by now), at the same time coupling with unprecedented scientific developments that are rapidly allowing an extreme personalization of cures – and disease designs («salami slicing strategies»).
- Please note: because of the incentives' structures, «repurposing» of already available drugs as ODs became a solid trend, as well as so-called «secondary orphan» approvals.
  - First-time orphan approvals have more than doubled over the past decade, with a record 37 of them in 2015. These approvals include new molecular entities, other new drugs and repurposed drugs approved as orphans for the first time. But companies continue to get secondary orphan approvals to treat additional diseases — or sometimes just slices of those diseases.
- Moreover, new ODs come at a cost: in fact, such products show skyrocketing average prices (Novartis' Zolgensma being only the most recent case hitting the frontpages).
- Because of that, ODs are increasingly challenging the sustainability of public pharmaceutical expenditure plans: ODs costs are predicted soon to consume 6-8% of healthcare budgets of the larger EU countries.

THE ORPHAN DRUGS SCENARIO



Source: EvaluatePharma, *Orphan Drug Report*, April 2019

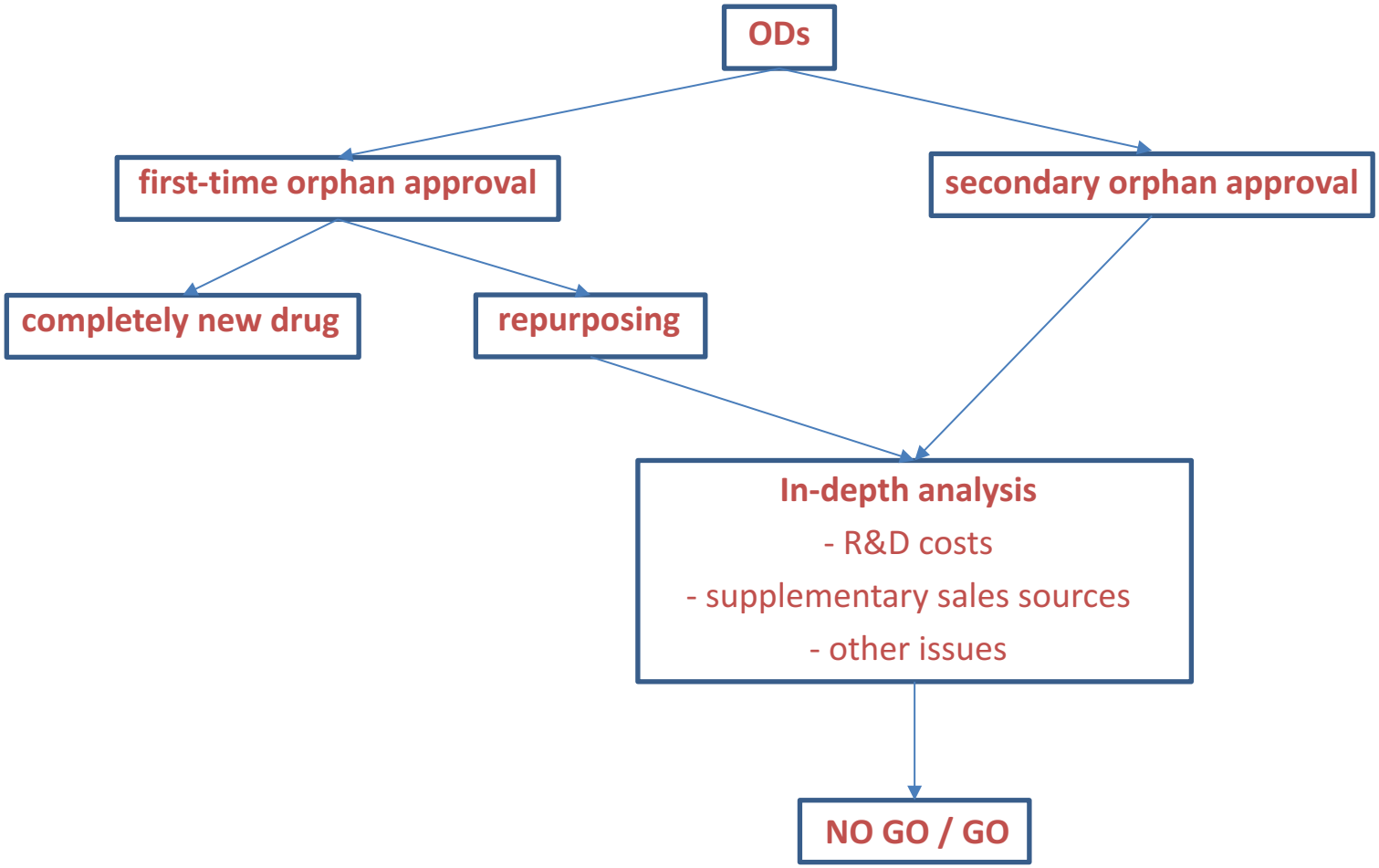
THE ORPHAN DRUGS SCENARIO: REMARKS

- An important *caveat*: cost awareness might not be enough…
  - «[…] *To state the point: products with high fixed costs are not characterized primarily by 'cost-determined prices', as is the usual economic model and common-sense intuition; instead, they are characterized by 'price-determined costs', in the sense that increases in the demand for or value of new products* […] *will make it rational for profit maximizing firms to incur higher fixed costs. So the cost of developing a new product, whether it is $1 billion as industry friends suggest or much less as its critics suggest, has nothing to do with the prices at which those products are initially offered; prices depend on willingness to pay and costs of production.* […] *As is well known, the markup of price over marginal cost will depend on the demand elasticity, and so much of the economic explanation of any variation (across products or over time) in the prices of new products must be a story about variation in demand elasticity.*» (M.Pauly, *Commentary. Drug and Vaccine Pricing and Innovation: What is the Story?*, in Managerial and Decision Economics, 2007, p. 408)
- … But it definitely helps. As a consequence, the path established by the WHO resolution must be followed (and deeply improved).

THE ORPHAN DRUGS SCENARIO: QUESTIONS AND REMARKS

- Now, a general question: what kind of innovation do we want to protect and support?
- In fact, genuine and worthwhile innovation is the one that brings completely new products on the market: it is doubtful that many secondary orphan approvals to treat additional/*sliced* diseases show such innovation.
- Also, a costs/price relationship analysis (costs + reasonable profit margin) should take into consideration the effective level of R&D costs. When such costs might not exist or be very limited, as in case of repurposing and – again – secondary orphan approvals, aggressive pricing strategies should be challenged.
- Finally, the impact of public funding on the costs' structure of both «pre-» and «post-marketing» product development should be taken into due consideration for establishing sustainable prices and adjusting them along the product cycle management.

THE ORPHAN DRUGS SCENARIO: A TENTATIVE ANTITRUST ROAD-MAP



«DRUGSPLOITATION»? VERY RECENT NEWS

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A524 - Avviata istruttoria sul farmaco di Leadiant per la cura della xantomatosi

COMUNICATO STAMPA

L'Autorità Antitrust ha deciso di avviare un'istruttoria nei confronti delle società Essetifin S.p.A., Leadiant Biosciences S.p.A., Leadiant Biosciences Ltd., Leadiant GmbH e Sigma-Tau Arzneimittel GmbH, appartenenti al gruppo Leadiant, per verificare l'ipotesi di un abuso di posizione dominante sul mercato italiano della produzione e vendita dei farmaci a base di acido chenodesossicolico (CDCA) per la cura di una malattia rara: la xantomatosi cerebrotendinea. Secondo quanto ipotizzato nel provvedimento di avvio, Leadiant avrebbe posto in essere un'unica e articolata strategia avente il fine di precludere l'accesso dei concorrenti al mercato della produzione di farmaci a base di CDCA e di imporre prezzi ingiustificatamente eccessivi per la vendita del proprio farmaco, contenente tale principio attivo, denominato *Acido Chenodesossicolico Leadiant*.

In particolare, sembrerebbe che il contratto di fornitura in esclusiva di CDCA stipulato da Leadiant con l'impresa chimica Prodotti Chimici ed Alimentari S.p.A., una delle principali produttrici di tale principio attivo, impedisca alle aziende ospedaliere che possono eventualmente richiedere alle proprie farmacie di allestire una produzione galenica di farmaci a base di CDCA, di ottenere la materia prima necessaria per la produzione dei farmaci per la cura della malattia rara. Inoltre, sembrerebbe che, una volta ottenuta l'autorizzazione all'immissione in commercio per l'*Acido Chenodesossicolico Leadiant*, Leadiant abbia posto in essere un comportamento dilatorio e ostruzionistico volto ad ottenere nella negoziazione con AIFA un prezzo di vendita molto alto per tale prodotto, nella consapevolezza che sul mercato non vi possono essere altri farmaci sostituibili.

Source: ICA's website, 15 October 2019

https://www.agcm.it/media/comunicati-stampa/2019/10/Avviata-istruttoria-sul-farmaco-di-Leadiant-per-la-cura-della-xantomatosi

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«Noi dovremmo sentire l'ambizione di conoscere ciò che è reale non solo redigendo l'inventario dell'esistente, ma definendo in più che cosa avrebbe potuto esistere, cosa potrebbe esistere, e cosa potrebbe venire in essere.»

(R. Sacco, *Antropologia giuridica*, Bologna 2007, p. 45)

THANK YOU

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