DECLARATION FOR THE PhD THESIS

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January 31, 2011

Aura Bertoni

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INTRODUCTION

As innovation incurs in technological changes, innovators adapt their approach to research in order to take full advantage of scientific progress. As the legislative and judicial branches respond to science advance, these new regulations of technical information impact on further innovation development. In this reciprocal exchange, old and new patent problems arise afresh. In particular, the advent of biotechnology has been accompanied by closer relations between academia and industry, in order to ensure that inventions would go out from university laboratories and benefit society as a whole.

The commercial involvement of academic research was supported by the patentability of its outputs, and, later on, "knowledge industries" pushed governments towards a strong worldwide reliance on proprietary rights for spurring innovation. Whereas mere economic incentives and typical static distortions of the patent system cause allocative problems, also in research agenda, new dynamic distortions, like patent proliferation and blocking patents, are likely to inhibit follow-on research, and so, to breach the traditional "social contract" between governments and patentees for innovation enhancement. Even more often, old-fashioned "check and balance" mechanisms of patent law are revealing not adequate

for the modern face of biomedical innovation and, while a re-balance between private and public interests in patents is more and more urgently required, new or renewed means need to be explored and applied.

Monopolies, externalities, information problems are examples of market failures. Since they engender economic inefficiency and distributional inequities, the public interest often requires state regulation to correct them. However, governments may decide to delegate the regulatory authority to private ordering and to articulate, within public law, efficiency and non-efficiency policy aspirations for which private actors act. In this context, intellectual property is acknowledged as a public good for being non-rival, the use by one person of it does not diminish the use by an another one, and non-excludable, its possession or use does not preclude others from possessing or using it as well, and, as a consequence, there may be no incentive to bear the costs of its creation. In this sense intangibles, such as technological information, are a clear example of market failure.

Recognizing that innovation incurs into the danger of under-production and owns an essential role in social welfare and economic progress, western legal systems have increasingly granted property rights on the products of technical and scientific knowledge with patents. According to neoclassical economic arguments, patents secure a "social

contract" between national governments and patentees conferring limited monopolies to the patent owners for a 20-year period in exchange for the disclosure of their inventions and, in turn, increased innovation.

By itself, patent system is, thus, traditionally identified as a tradeoff between static efficiency, which requires wide access to knowledge users at marginal social cost, and dynamic efficiency, which depends upon incentives to invest in innovation for which the social value exceeds development costs. For balancing the public interest in the access to useful innovation with the private interest in the exercise of property rights, national governments impose a number of public ordering safeguards, not only in term of patentability requirements but also setting monopolistic powers limitations. In other words, while patent law employs market incentives to correct the market failure of underinvestment in intellectual products, the existence of internal flexibilities already implies the acknowledgment that it is a non-complete solution.

More precisely, patents introduce economic distortions since they grant patentees an exclusive right to control the commercial exploitation of their inventions, which permits them to set monopolistic prices on patented products. The supra-marginal prices and the reliance on mere economic incentives for spurring innovation entail that patent system may also produce allocative distortions, in both access and creation of

knowledge. Considering that private patents rights are designed to maximize the aggregate welfare in innovation enhancement, distributive concerns have been generally taken into consideration, but only into imposed public safeguards, like the flexibilities incorporated into patent regimes.

Nowadays patents go beyond this standard tradeoff introducing also dynamic distortions. The exclusive right of the patent owner permits him to prevent others from using his invention, mainly with restrictive licensing or refusal to license practices. With regard to fields, like biomedicine, based on cumulative and complementary research, such exclusivity, when declined into exclusionary, may inhibit the development of follow-on innovation if that patent covers essential features of the invention which cannot be invented around and, therefore, trigger a so-called blocking patent.

Emblematic to explain how patents and restrictive licensing practices may harm the transfer and dissemination of technology is the *Myriad* case in research and clinical genetics. In the early 1990s two major genes, BRCA1 and BRCA2, in which germ line mutations cause breast and ovarian cancer susceptibility, were identified thanks to a number of academic scientists, and then cloned and sequenced by the industry, precisely by the enterprise Myriad Genetics Inc. Several patents were granted to

Myriad for these two genes and later on diagnostic tests for mutation detection were developed by that company. Myriad's policy of not licensing those blocking patents, or doing it at not acceptable conditions by academic laboratories, meant that all tests would have had to be performed in its own laboratories. This choice was strongly contrasted by European geneticists, both ignoring patents, and so continuing to practice different BRCA tests, and objecting Myriad's patents at the European Patent Office (EPO). Their American fellows had not the same strength since the United States Patent and Trademark Office (USPTO) does not allow a similar opposing procedure, and for the reason that the fear of patent infringement lawsuits was enough to deter them from further in-house testing.

Therefore, it is evident that proprietary rights, even on a single gene, pose serious risks as, among others, they may cause both substandard quality of gene testing, and barriers to subsequent research on that gene, and for multi-gene based disorders as well. In addition, the emerging use of genetic markers as predictors of drug efficacy and toxicity in *pharmacogenomics*, a new branch of pharmaceutical research, although it represents a promising tool for optimizing drug development, would be affected by the adverse effect of gene patenting.

Some of the institutional and technological changes of last years,

above all the “commercialization” of academic research, together with biotechnology and gene patenting, have driven to an ever increasing number of patents. Despite this phenomenon is considered as a good index of innovative activities, it might weight down the burden of patent law distortions. Such ongoing process of patent proliferation may represent the last straw in the landscape of patent failures. In fact, when patent proliferation combines with the static distortion of monopolistic prices, a royalty stacking problem arises. At the same time, when a multitude of patent owners hold multiple blocking patents, “patent thickets” are likely to emerge, and hinder accessibility to patented technology.

Furthermore, we may fall into patent failures also within pharmaceutical research, a field in which it is quite frequent to find polarized viewpoints because of the extraordinary importance of what its industry produce, namely medicines, and for the peculiar characters of its production process. In fact, on one hand a drug is simply a specific formulation of active ingredients, developed for therapeutic purposes and sold in the market as commercial product. One the other hand, considering the crucial role of certain drugs for the cure of highly sensitive diseases and for global health, with special reference to essential medicines, they cannot be considered as “ordinary” goods. It goes without

saying that closing the "health gap" between rich and poor nations and eradicating the "diseases of poverty" is a hard task, in particular for the so-called neglected tropical diseases. The existence of proprietary rights at upstream level may increase costs associated with the overall drug R&D, and so creating even higher obstacles for neglected diseases given their low-commercial-value and the failing incentives to invest that patents give in this research area.

It is then that nature, regulation and functions of patents in the idiosyncratic area of biomedicine serve as an emblem of tensions and convergences between private and public spheres, their traditional responsibilities and new legal instruments employed to pursue their respective goals. Exactly within this distinctive conjunction of public and private interests into patent law, private ordering flexibilities like open source models are revolutionising the intellectual property landscape since providing a new way for reconciling these competing, and often conflicting, interests. In fact, the essence of open source approach is that the self-interest of each knowledge developer combines with the norm of sharing a public good such as knowledge itself. Even if this movement started within the computer programming field, mainly covered by copyright protection, then it has appeared as a promising solution also for obstacles created by patent distortions in biomedical and pharmaceutical

research.

Chapter I of my work discusses traditional justifications and collateral functions of patents, explains typical and emerging trade-offs of the patent system and, with a specific focus on biomedicine, explains the reasons behind the need of flexibilities. Chapter II is targeted on biomedical patents and their mutated role into upstream research scenario. Shortcomings of current public law flexibilities in mitigating economic and allocative distortions within biomedical R&D will be also illustrated, together with an early assessment of the use of open source models as private complementary flexibilities. Chapter III delineates the problem of the tropical neglected diseases as a clear example of patent failure and explains which alternative incentives have been constructed to spur drug R&D. Chapter IV concretely examines ongoing open source initiatives along the biomedical research course, from upstream to downstream level, illustrating in which areas of this research field is desirable the use of such models, and the essential characters they need to have in different stages of research development. The concluding remarks show how open source philosophy may, at the same time, constitute a private ordering flexibility of patent rights and a scheme with normative force, since introducing inside the intellectual property regime a norm of sharing knowledge, where in the past exclusion and control were

deemed natural and essential, for the promotion of its own development. It is then that the traditional sharing norms of science, partially lost through the "propertization" of upstream research, have an original opportunity to be restored by "privatizing" patent regulation.

CHAPTER I

JUSTIFYING PATENT RIGHTS IN CONTEMPORARY BIOMEDICINE

I.1) THE CHANGING NATURE OF NATURAL RIGHTS-BASED JUSTIFICATIONS IN PATENT LAW

It is well known that for seeing the first example of patent system we have to look away back in 14741. The Republic of Venice decided to recognize a ten-year monopoly right to inventors 'from diverse parts' so that 'more men would then apply their genius, would discover, and would build devices of great utility for [their] commonwealth' and 'who may see [that devices] could not build them and take the inventor's honor away'. From this comes that in patent genesis there was a clear public policy substrate. However, the moral interest of inventors, or else the “honor”, was also considered2, even if in an unequivocally complementary and

1 In truth, the propertization of intangible goods, with its inherent incentives dimension, dates back at least to the third century BC in the practice of the Greek city-state of Sibaris. As documented by Athenaeus in his *Deipnosophists,* 'if any caterer or cook invented a dish of his own which was especially 'choice', it was his privilege that no one else but the inventor himself should adopt the use of it before the lapse of a year, in order that the first man to invent a dish might possess the right of manufacture during that period, so as to encourage others to excel in eager competition with similar inventions': *see* Axel Gosseries, *How (Un)fair is Intellectual Property?, in* INTELLECTUAL PROPERTY AND THEORIES OF JUSTICE 15 (Axel Gosseries, Alain Marciano and Alain Strowel eds., Palgrave Macmillan, Basingstoke, 2008).

2 Giulio Mandich, *Venetian Patents (1450-1550),* 30 JOURNAL OF PATENT OFFICE SOCIETY 166, 176-177 (1948).

instrumental manner, having primacy the social end of enhanced innovation.

Nonetheless, within the traditional justifications for intellectual property (IP) protection we may find various hints to the natural rights doctrine. Though they are frequently grounded on an ethical dimension, all of them are particularly directed to guarantee creators of intangibles moral rights to control their work, a fair and equal share, and to accentuate the individuality of creations originating from any private person.

German copyright law was mainly inspired by the arguments expressed by Kant and German Idealism philosophers. Immanuel Kant identified a 'natural obligation' to respect the author's ownership of his work3. In this way, the role of authorial personality becomes crucial for the protection of authors' works, and the ethos of human rights law as translated into the German Constitution is linked to intellectual property4. In any case, and more in general, the relevance of creator's personality is self-evident in all the Civil Law jurisdictions, starting from the basic

3 Immanuel Kant, *Of the Injustice of Counterfeiting Books, in* ESSAYS AND TREATISES ON MORAL, POLITICAL AND VARIOUS PHILOSOPHICAL MATTERS 225, 229-30 (1798).

4 *See,* for instance, the right issued by the German Law on Copyright and Related Rights 1968 allowing the author to control how his work in perceived by the public and the tight relation with Articles 1 and 2 of the German Constitution where the rights to human dignity and free development of personality are individualized: GRAHAM DUTFIELD AND UMA SUTHERSANEN, GLOBAL INTELLECTUAL PROPERTY LAW 55-56, 62 (Edward Elgar Publishing, Cheltenham-Northampton, 2008).

consideration that they preserve the "author's rights" (such as the legislation of the *droit d'auteur* in France or the German *Urheberrect*) instead of granting a "copyright" in which it is emphasized the right to limit public's right to make copies5.

Whereas the role of moral rights appears more intuitive for the artistic and literary property granted by copyright law, their relevance is less straightforward for patent protection. Inventions, in order to become industrial property, must meet a few internationally recognized standards, namely novelty, inventiveness (non-obviousness in the US) and, of course, industrial applicability (usefulness in the US), all of them demonstrating that economic rationales for any patent system are more than manifest. At any rate, within the theory of intellectual property it is not hard to find attempts to enrich the social and economical elements of innovative activity with moral values.

The French Enlightenment developed a distinguishing theory of intellectual property thanks to which non-tangible information goods were recognized as pertaining to the "right of man". This is precisely illustrated by the Preamble of the French Industrial Property Statute of 1790 in which is stated that "any new idea, the manifestation or development of

5 Peter S. Menell, *Intellectual Property: General Theories,* in 2 ENCYCLOPEDIA OF LAW AND ECONOMICS 156 (Boudewijn Bouckaert and Gerrit de Geest eds., Edward Elgar Publishing, Cheltenham-Northampton, 2000).

which may become useful to society, belongs basically to the one who has conceived it, and that it would be a violation of the Right of Man, in their essence, not to regard an industrial discovery as property of its author"6.

Again in France, but in the aftermaths of the Word War I, there was the first movement for ensuring property rights to scientific discoveries, as part of the larger front encouraging a *droit de suite7* or a set of moral rights for creators. This movement formally manifests itself in 1922 when the law professor and member of the chamber of deputy J. Barthélemy proposed to abrogate Article 30 of the French Patent Law of 1844 attesting nullity and voidness of all patents on "principles, methods, systems, discoveries and theoretical or purely scientific conceptions of which no industrial applications are indicated8. The fundamental assumption of his proposal was that justice compels to provide creators a share in benefits created by their intellectual activity.

In short, other than affording a wider protection to inventions, Barthélemy's proposal is directed to recognize the right of scientists in

6 Law on Useful Discoveries and on Means for Securing the Property therein to the Authors, adopted December 31, 1790; enacted January 7, 1791, *quoted in* Frank D. Prager, *A History of Intellectual Property from 1545 to 1787,* 26 JOURNAL OF THE PATENT OFFICE SOCIETY 711, 756 (1944).

7 The *droit de suit* is a reinforced protection in favor of artists and their legal representatives according to which who sells his work may "follow" it in its subsequent public sales, for collecting royalties on the sale price, during the time of the copyright: *see* STEPHEN P. LADAS, PATENTS, TRADEMARKS, AND RELATED RIGHTS: NATIONAL AND INTERNATIONAL PROTECTION 1850 (Harvard University Press, Cambridge, 1975).

8 Quoted in Stephen P. Ladas, *The Efforts for International Protection of Scientific Property,* 23 THE AMERICAN JOURNAL OF INTERNATIONAL LAW 552, 553 (1929).

their discoveries, and it comprises two groundbreaking ideas. Above all, in case an ordinary patent is not obtainable, any scientist should have the right to economic remuneration once his theoretical discovery obtains a practical application. Moreover, the proposal provides the insertion of a new type of right for protecting scientific discoveries, the so-called "patent of principle". By virtue of this distinct right, a scientist would not have an exclusive right to make or use the discovery as per ordinary patents, but only the right to royalties in view of compulsory licenses granted to whom is interested on the practical application of that discovery9.

The moral profile incidental to the patent of principle proposal is instead represented by its closeness to copyright discipline. In fact, the length of protection is the entire life of the discover plus fifty years. Besides, there is the absence of any formality for the grant of this right to scientists, since existing from the time of the discovery. Contemporaneously, in case an author of inventions or discoveries obtains an ordinary patent, and after the term of protection expires, he only loses the legal monopoly, *i.e.* the exclusive right status, but he maintains the opportunity to file a "patent of author". This additional type of patent is directed to preserve the right to royalties claims, further to the use of the

9 LADAS, PATENTS, *supra* note 7, at 1851.

invention for all the life of the inventor and fifty years after his death10.

The Committee on Intellectual Cooperation of the League of Nations became acquainted with Barthélemy's proposal and the drawing CTI *(Conféderation des Travailleurs Intellectuels)* project on the protection of scientific discoveries. On August 5, 1922, that Committee decided to appoint as rapporteur for a study on scientific property Senator F. Ruffini who, amongst the primary considerations he gave on this matter, exactly highlighted the moral aspect of justice in rights on scientific discoveries11. In answer to Ruffini's considerations, the Vice-Director of the United International Bureaus of Intellectual Property, Professor Gariel, proposed its own plan for addressing the problem of the protection of scientific conceptions. This last plan, although not in favor to a scientist's individual property right, suggests that a reward should be paid him because of the labor he supplies12.

The reasoning in support of Gariel's plan for the economic compensation of individuals involved in scientific research evokes an

10 *Id.* at 1856.

11 'In all countries, as will be seen, legal theory, eve n when it emanates from authors of the highest repute, has hitherto failed to explain so strange a phenomenon, except by inadequate or purely utilitarian reasons. […] It appeared to us, in the first place, that it was perhaps one of the duties of an organization of a great institution, such as the League of Nations, for establishing universal justice to study the problem and to propose means of putting an end to so flagrant an injustice. *There is a great work of justice to be done and an ill to be redressed* (emphasis added)': *see* F. RUFFINI, REPORT ON SCIENTIFIC PROPERTY 1 (Committee on Intellectual Cooperation, Doc. A. 38, XII, 1923).

12 LADAS, PATENTS, *supra* note 7, at 1862.

another "moral" approach commonly used for justifying intellectual property, namely the Locke's labor theory of property. Locke, as a natural law theorist13, has inevitably been mentioned in a lot of legal studies and many of his works have been applied inside the patent field. Even if the real pertinence to intangibles would more probably lay in his distinction between positive and negative community, or else between a community where the commons is owned by all and another one where the commons is open to ownership by all, his importance within the theory of intellectual property is more generally linked to the labor theory of property14.

According to Locke, the property right in something that a person produces with his own efforts emanates from property right in his body. Because a person owns his body, he owns what it does, namely his labor. The creation of property by Locke, i.e. the partition of the world into bundles of exclusive control, is driven by a practical problem since 'men, being once born, have a right to their preservation, and consequently to meat and drink, and such other things, as nature affords for their

13 The natural right character of his theory of propriety implies that such theory is based on a notion of entitlement rather than on desert or on incentive, therefore it cannot be adjusted with the reward element for its justification: *see* Daniel Attas, *Lockean Justifications of Intellectual Property* 30, *in* INTELLECTUAL PROPERTY AND THEORIES OF JUSTICE, *supra* note 1.

14 PETER DRAHOS, A PHILOSOPHY OF INTELLECTUAL PROPERTY 54-57 (Ashgate Publishing, Aldershot, 1996).

subsistence'15. In contemporary society the concept of subsistence is truly weak in order to fix a general justification of property because it can only justify the consumption of goods, and of a quite limited range too. Thus neo-Lockean simply try to put it apart and they appeal to other relevant values, like the need for any person to set long-term life plans16 or the danger of a tragedy of the commons17. In spite of the fact that Locke's *Two Treaties of Government* only tackle tangible property and that the labor theory is nowadays a too vague basis for establishing a strong justification to property for "abstract objects", these arguments bestow a "powerful totem" for the defense of intellectual property rights as well18.

The translation of Locke's labor theory into the specific patent realm originates a principle upon which the person who invests his labor for creating an invention is morally entitled to the resulting products, or else he has a moral right to private property19. Using the concept that

15 John Locke, *Of Property, in* TWO TREATIES OF GOVERNMENT ¶ 24 (Cambridge University Press, Cambridge, 1960/1968) (1689).

16 The interest precisely consists in the ability to use the object in the furtherance of one's life plan and it permits to extend the allowed goods to a broader range: *see* Attas, *supra* note 13, at 32, *citing* LOREN LOMASKY, PERSONS, RIGHTS, AND THE MORAL COMMUNITY (Oxford University Press, Oxford, 1987).

17 This metaphor refers to those situations in which occurs an overuse of shared resources because too many owners have 'privileges of use' and no one has 'rights of exclusion': *see* Garrett Hardin, *The Tragedy of Commons,* 162 SCIENCE 1243 (1968); *but cf.* Bruce L. Levine, *The Tragedy of the Commons and the Comedy of the Community: The Commons in History,* 14 JOURNAL OF COMMUNITY PSYCHOLOGY 81 (1980) noting how the historical experience demonstrates that whereas the commons are not owned by anyone, they can be regulated by the community instead.

18 PETER DRAHOS, A PHILOSOPHY, *supra* note 14, at 48.

19 A. Samuel Oddi, *TRIPS – Natural Rights and a "Polite Form of Economic Imperialism,*

'everyone has an inalienable right to his labor', there have been developed many syllogisms, of varying validity, conferring exclusive rights to inventors but also, much more indirectly, for inventor's employers, both corporations and universities, and employer's sponsors, or else investors20. Hence, the application of Locke's labor theory, although already not much pervasive for individual innovative activities, has been extended in an even more instrumental way for the protection of investment-based intangible goods21.

It is a matter of fact that in the late of Seventies the most research-intensive industries of the US like computing, electronics but most of all pharmaceuticals, pushed to change "knowledge game" rules22. Drahos defined this game as an organized play addressed to propertize as much knowledge as possible. However, as conditions of the game change, key players have to change the rules of the game for continuing to win. Most

29 VANDERBILT JOURNAL OF TRANSNATIONAL LAW 415, 427-28 (1996).

20 The moral right to the product of one's labor also means obtaining the right to possess and personally use it for his own benefit. However, this right does not coincide with the right protected by patents to sell the invention in a market and exclude others: *see* Edwin C. Hettinger, *Justifying Intellectual Property,* 18 PHILOSOPHY AND PUBLIC AFFAIRS 31, 39-40 (1989).

21 DUTFIELD AND SUTHERSANEN, *supra* note 4, at 54-55.

22 The insights of public choice theory have been applied to scrutinize the political process producing intellectual property legislation. It is worth noting that Olson points out that this type of legislation cannot move forward without consensus but, at the same time, who stand to gain concentrated benefits (namely, intellectual property owners) may prevail in legislative for a, both national and international, over those who stand to bear diffuse costs (i.e. users): *see* Thomas P. Olson, *The Iron Law of Consensus: Congressional Responses to Proposed Copyright Reforms since the 1909 Act*, 36 JOURNAL OF THE COPYRIGHT SOCIETY OF THE USA 109 (1989).

notably, their efforts were directed to establish a tie between the trade regime and investments and, in turn, to translate investments into globally enforceable intellectual property rights. The task of setting this kind of strategy was definitely not a child game, considering intellectual property protectionist history and its monopolistic nature, always of legal origin, at times with economic characters too. Therefore, it was unthinkable that those "knowledge cartels" could have gone to the federal government asking for stronger intellectual property protection, in a way to face their increased R&D expenditures and competition from foreign manufacturers, without an at least apparent legitimate justification. One of the leading lobbyist, the pharmaceutical company Pfizer, was right on target by means of think tanks, or else directly funding studies and conferences carried out by these entities, in which the frame of reference were essential liberal values, such as the individual right of property, the right to a reward for labor, and fairness23.

Concretely, there are three major problems for applying the Locke's theory of property to the sphere of intangibles and all stem from the nature of such goods itself. Firstly, since ideas are non-rival, they can be used simultaneously by everyone without diminishing either their use-value or exchange-value. Secondly, there are also difficulties as for the

23 PETER DRAHOS WITH JOHN BRAITHWAITE, INFORMATION FEUDALISM 59-70 (The New Press, New York, 2002).

application of Locke's principle of appropriation. In its positive significance, it implies the ownership of ideas, as products of the mental labor. However, the more advanced is a society, the more ideas are externally influenced. There seems to be no natural way to identify the individual originator of an idea, who it may be only conventionally determined. Finally, in its negative significance, there is the mirror image of origination, that is the identification. Also in this context there is not a natural way to draw the line between the first and the many secondary expressions of an idea originating, for example, by imitation or inspiration. Neither it is possible for abstract and specifically applied ones, or between similar independent ideas. All these boundaries are not evident in nature and require consequentialist arguments for their definition24.

According to a Lockean perspective, it is also generally true that the ownership, and so control, of ideas originating in our minds when they are in other minds would violate others' right to control the contents of their mind. On the other hand, we may imagine a community of owners in which it exists the norm of not depriving anyone. Necessarily, in that community the exclusive control deriving from property will not be exercised by each owner in a way to violate the right to control of the

24 Attas, *supra* note 13, at 35-53.

others. In such circumstances the use of intellectual property would be complaint with Locke's theory.

There is a community matching with these characters and this might be a reason behind the recent reference to Locke's theory of property by the open source software (OSS) movement. OSS is a model of innovation characterized for combining forces of countless programmers from all over the world and for having wide dissemination of knowledge, rather than the conventional model of exclusion, as primary focus. Lockean arguments have been linked to the ownership aspect of OSS. In fact, it has been maintained that any potential way to obtain ownership of an open source project, and each following derivative work, has hackers' labor as generator. Along with this viewpoint, open source developers putting their labor into programming projects should still expect a return in terms of ownership from their efforts, although not for exclusionary purposes25. OSS employs intellectual property in an unconventional manner, namely as a way to avoid that innovators, after putting their labor upon the OSS platforms, may assert property rights in order to exclude others26.

More generally, even downsizing this extended reliance on Locke's theory of property, since it is essentially too indeterminate and its use is

25 Eric S. Raymond, *Homesteading the Noosphere* 6-9 (Thyrus Enterprises, 2000) *available at http://citeseerx.ist.psu.edu* (last visited December 20, 2010).

26 *See* Josh Lerner and Jean Tirole, *The Simple Economics of Open Source,* 50 THE JOURNAL OF INDUSTRIAL ECONOMICS 197 (2002) where it is admitted that ordinary economic models have not well adapted to explain this phenomenon.

mainly generated by the pursuit of giving ideological legitimacy to pragmatical goals, other Lockean arguments, as suggested before, may still make sense and offer a valuable point of reference for a sort of balance test in patent law. In fact, in the light of Locke's conceptions of community and intellectual commons27, the reward to any laborer-inventor has to adjust with the maintenance of the commons since "no loss to others" is an essential precondition for the acquisition of property rights28. According to Locke's 'proviso', everyone has a right to work on initial common resources but later these resources, or their improved equivalents, have to return to the commons for permitting others to use them29. Moreover, as additional condition for a legitimate obtainment of property, Locke requires that individual property would not imply "spoilage". In other words, a laborer must not worse others' opportunity to appropriate resources, but also he must not take more than he can

27 As pointed out by Drahos, the commons is a legal concept characterizing the English property law. In Locke's time the commons referred to rights of persons in relation to another's land. This concept did not refer to a public ownership of that land, on the contrary to a right of access to the commons for those purposes connected with the exercise of related rights. It derives that this legal conception was a truly territorial or, anyhow, a group-specific one, and it did not refer to something to all humanity has right to access: *see* DRAHOS, A PHILOSOPHY, *supra* note 14, at 54-56. In this sense, 'intellectual commons' idea may be opposed to 'intellectual property' in terms that the former refers to abstract objects already owned by a person against whom the commoners have rights, instead in the latter case the owner has an exclusive right with reference to those objects.

28 *See* Hettinger, *supra* note 20, at 44.

29 DRAHOS, A PHILOSOPHY, *supra* note 11, at 54-68.

use30.

Therefore, in case Lockean assumptions are adduced by someone as a bargaining chip to get theoretical foundations to purely and not steady utilitarian justifications in patent law, at that point he would have to consider both sides of the coin, or else the overall range of Locke's property theories, for obtaining a reasonable legitimization.

As a consequence of this prerequisite, and in compliance with the labor theory of property but also with the characterizations of community and commons, any intellectual commons erosion in favor of any inventor's benefit, it would not be acceptable31. Focusing on patent rights, unduly restrictions on access to patented products make likely that erosion. Therefore, a public duty to guarantee the right to expend labor on such intellectual commons by any new potential inventor implies the need to avoid that erosion. In addition, any patenting and licensing practice which prevents beneficial uses of the patented product for other inventors should not be allowed.

In more concrete terms, for instance, if the patent owner of an essential tool in biomedical research asserts exclusivity in a way to prevent its access to other laborers-inventors, directly denying the use of

30 Hettinger, *supra* note 20, at 44.

31 Jeremy Waldron, *From Authors to Copiers: Individual Rights and Social Values in Intellectual Property,* 68 CHICAGO-KENT LAW REVIEW 841 (1992-1993).

that tool, or indirectly fixing not acceptable license terms, he produces an erosion of intellectual commons for the scientific community. In fact, he may prevent the use of original resources upon which that patented good was built up and locked into the patent claim. Moreover, he impedes the development of further innovation by others on the basis of his invention.

Besides these so-called "blocking patents", Eisenberg and Heller have suggested that economic efficiency in biomedicine may be impaired by excessive division of intellectual property rights32. The recent expansion of propriety rights in life sciences, by the mean of the proliferation of patents on genes, biological pathways and stem cell lines, with multiple and heterogenous holders, might render difficult for each laborer-inventor to acquire all the necessary rights. In absence of agreements for licensing or assigning such rights, which may permit the access to the relevant scientific commons, science might incur in an underuse of valuable knowledge. The magnitude of that waste depends on how much benefit those patented products would bring to those who are excluded from their use33.

32 Michael A. Heller and Rebecca S. Eisenberg, *Can Patent Deter Innovation? The Anticommons in Biomedical Reseach,* 280 SCIENCE 698 (1998); for an extended explanation of the 'tragedy of anticommons', *see* MICHAEL HELLER, THE GRIDLOCK ECONOMY 1-22 (Basic Books, Perseus Books Group, 2008).

33 On this last point, *see* Hettinger, *supra* note 20, at 45.

I.2) THE COMMODITIZATION OF BIOMEDICAL RESEARCH FROM AN HEGELIAN PERSPECTIVE

The previous account of the *droit de suite* movement and its subsequent extensions both within France, due to the influence of Barthélemy and the succeeding contribution of the CTI, and internationally, thanks to the interest expressed by the Committee on Intellectual Cooperation of the League of Nations, shows that scientific property is probably a never-ending story rooted into a distant past.

Nowadays, the characterization of scientific knowledge "propertization" generally also implies extensive discussions, among other things, about a dangerous deficit of freedom for academic research associated with pro-commercial climate in universities.

Curiously Hegel, a theorist who represents an another powerful alternative to Locke for justifying intellectual property, instead considered property as the first embodiment of freedom. In Hegel's personality theory of property, an individual attains self-knowledge of himself as a free person through an absolute right of appropriation. Since personality should be left free, in principle there are no prior restrictions on what can or cannot be "propertized"34. At large, private property, actualizing the

34 DRAHOS, A PHILOSOPHY, *supra* note 14, at 78, where he clarified that, along with this

'will' of any individual, would permit him to control his internal and external world, and notably intellectual property should also satisfy the peculiar need of guaranteeing holders against thievery. In other words, property rights define legal boundaries for any intellectual good, so permitting to not be stolen by others, and to be recognized by others, as element for future creations35. Starting from Hegel's perspective as well as from Kant's Philosophy of Law, Margaret Radin developed the personhood justification for property suggesting that the premise to this theory is the individual's need of some control over resources pertaining to the external environment. The necessary assurances of control take the form of property36.

As constituting an individual's 'own private personality', intellectual property would not be alienable in Hegel's view37. However, since he himself recognized that products of mind may become valuable 'things', third parties should come into possession of these things so as to produce

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reasoning, patenting of transgenic animals or human life forms, like DNA fragments, should be possible insofar they are appropriable.

35 *Id.* at 82.

36 Margaret J. Radin, *Property and Personhood,* 34 STANFORD LAW REVIEW 957, 957 (1982). Later on the commentator discussed this perspective in relation with the significance of market inalienability and its justifications: *see* Margaret J. Radin, *Market-Inalienability,* 100 HARVARD LAW REVIEW 1849 (1987).

37 'Some goods, or rather substantive phases of life are inalienable, and the right to them does not perish through lapse of time. These comprise my inner personality and the universal essence of my consciousness of myself, and are personality in general, freedom of will in the broadest sense, social life and religion'. *See* GEORG W.F. HEGEL, PHILOSOPHY OF RIGHT ¶ 66 (S.W. Dyde trans., Batoche Books, Kitchener 2001) (1821).

other numerous ones38.

Hegel acknowledged that individuals are members of civil society, hence property is not just an extension of their personality but, on the contrary, 'ideas' and 'things' become the subject-matter of contracts. Necessarily contract law is designed by the state, an institution devoted to serve individuals within civil society and to set the ethical life of the state itself so as to strengthen the community. This means that within the state there is space for property, but that it shall not be 'the private property of these or any other interests'. Because of that, Hegel found that the danger of intellectual property resides exactly in its utilization by civil society. As soon as civil society members become aware of pecuniary advantages of intellectual property, they will make pressure on the state in order to increase property rights on intangibles, a process starting inside national border but of international scale, since that it is the dimension of markets for the exchange of intellectual property goods39. Along this long course, these sort of "lobbying" initiatives undertaken by a national civil society may determine the ethical life of other

38 *Id.* ¶ 68. In particular, for Hegel, property is not alienable because of the concept of property as such, but rather 'the reason I can alienate my property is that it is mine only in so far I put my will into it. Hence I may abandon […] anything that I have or yield it to will of another […] provided always that the thing in question is a thing external by nature': see *id.* ¶ 65.

39 DRAHOS, A PHILOSOPHY, *supra* note 14, at 83-85.

communities40.

In line with these dangers, Hegel's theory makes reference to exceptions for teachers, plagiarism and modifications on inventions. In this sense it also works as an useful basis for the admittance of the so-called “flexibilities” to exclusive rights in copyright and patent law, and for conceding the use of intellectual property for improvements and derivative works41.

40 *Id.* at 88.

41 *Id. ¶* 69 in which Hegel states: Since the purchaser of such a product of mental skill possesses the full use and value of his single copy, he is complete and free owner of that one copy, although the author of the work or the inventor of the apparatus remains owner of the general method of multiplying such products. The author or inventor has not disposed directly of the general method, but may reserve it for his private utterance. *Note.*—The justification of the right of the author or inventor cannot be sought in his arbitrarily making it a condition, when he disposes of a copy, that the possibility of bringing out other copies shall not belong to the purchaser, but shall remain in his own hands. The first question is whether the separation of the object from the power to reproduce, which goes with the object, is allowable in thought, and does not destroy full and free possession (§62). Does it depend upon the arbitrary choice of the first producer to reserve to himself the power to reproduce or dispose of the product of his mind? Or, on the other hand, may he count it of no value, and give it freely with each separate copy?Now there is this peculiarity about this power, that through it the object becomes not merely a possession, but a means of wealth (see §170, and fol.). This new feature is a special kind of external use, and is different and separate from the use to which the object was directly appointed. It is not, as it is called, an *accessio naturalis* as are *foetura.* Hence as the distinction occurs in the sphere of external use, which is naturally capable of being divided, the reservation of one part, while another is being disposed of, is not the retention of an ownership without *utile.* The primary and most important claim of trade and commerce is to give them surety against highway robbery. In the same way the primary though merely negative demand of the sciences and arts is to insure the workers in these fields against larceny, and give their property protection.

I.3) Utilitarian Rationales for Patent Law: A Globally Interdependent Evolution

Although the globalization of intellectual public goods as well as the issue of technical and scientific knowledge "privatization" arrived with all their strength, in the first case, with the WTO (World Trade Organization) Agreement on TRIPS (Trade-Related Aspects of Intellectual Property Rights), and in the second one, after the advent of biotechnology, the question of the scope of patent rights and, especially, their role with respect to scientific production is unsettled since many more decades.

As for the first aspect, after World War II, beyond shadow of doubt, the US became the world's most powerful economy and started exploiting a comparative advantage in intellectual property-related goods. In 1989, the USTR (The Office of the United States Trade Representatives) declared that "no foreign country currently meets every standard for adequate and effective intellectual property protection"42, and the area of biomedical inventions was one of the most relevant given the growing weight of life science business into the US knowledge economy. As a consequence of pressure wielded by the pharmaceutical sector together with corporate copyright owners, the federal government of the US, on behalf of these

42 Quoted in Drahos with Braithwaite, *supra* note 23, at 94.

private actors43, promoted a trade-based intellectual property strategy. Such strategy had the long-term objective of pursuing a multilateral agreement on intellectual property, later known as TRIPS Agreement and, at the same time, it sets interim components such as bilateral negotiations and unilateral trade tools44.

In the context of biomedical "propertization", it is worth underling that both international patent rules and inherent national specifications are by definition technology-neutral since they do not distinguish between different technologies in setting legal standards of protection. Therefore, it is the concrete application of these standards which represents the key for differed results in practice. More precisely, within national legal systems, patent protection is generally granted (or not) and applied considering all the different features of each innovative context45. Recently, the arrival of a number of breakthrough technologies have contributed to the creation of "knowledge markets" in areas which were the privilege of non-market information exchange, so much so a "scope-colonization" of patents, and more generally of intellectual property rights, occurred.

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43 For an extended explanation of the role of the American-based private corporations and business associations in the shape of foreign and international intellectual property legislations: *see* SUSAN K. SELL, PRIVATE POWER, PUBLIC LAW 75-95 (Cambridge University Press, Cambridge, 2003).

44 DRAHOS WITH BRAITHWAITE, *supra* note 23, at 72-73.

45 With reference to the apparent paradox of 'a monolithic legal incentive for widely disparate industries', *see* Dan L. Burk and Mark A. Lemley, *Policy Levers in Patent Law,* 89 VIRGINIA LAW REVIEW 1575 (2003).

Among different countries there may be strategically distant or similar patent policies, and inherent judicial interpretations, even for a same given technological field46. A bright and prominent example is the *Harvard Oncomouse* case. In the US and Europe, both patent-granting offices and courts, at the beginning reached divergent conclusions as for the application of patentability standards to this first transgenic mice. While in the US it was already patented, in 1989 the patent application at the EPO (European Patent Office) was refused. However, in 2004, at the end of a long procedure of oppositions and responses, it was accepted, then moving closer American and European standards of patentability for biotechnological innovation. Further, for fear that European countries might ban patents on living organisms and genes, the European Commission decided to prepare the Directive on the Legal Protection of Biotechnological Inventions of which Article 3(2) specifically clarifies that 'biological material which is isolated from its natural environment or produced by means of a technical process may be subject of an invention

46 The TRIPS Agreement accommodates the technology-neutral character as well as the conditions for patentability deriving from western patent systems in Article 27(1) in which it is stated that 'subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced'.

[i.e. it is patentable] even if previously occurred in nature'47. This illustrates how in recent years this kind of "scope-colonization" in patent law coupled with an "indirect geo-colonization".

This case also demonstrates that the hot potato of property rights for scientific knowledge has changed hands over the years, moving from Europe to the US, and contours too. When it emerged in France it was a call for "scientific property" as third category of intellectual property rights, alternative to "literary and artistic property" and "industrial property". Precisely, the aim was to protect science outputs before their embodiment by the industry into patentable subject matters. Ironically, Thomas Ilosvay, in his article of 1953, criticized the US for the blatant indifference with regard to the appropriation of discoveries by scientists and called for a greater attention seeing the great hopes of modern science48.

With the appearance of new biotechnologies, we have seen that the issue of scientific property gained different characters, together with changed defenders. Whereas the purpose of the *droite de suite* movement was to find the way for what nowadays we would call a *sui generis* intellectual property system for scientific discoveries, the US was the first

47 European Parliament and Council Directive 98/44/EC of 6 July 1998 on the Legal Protection of Biotechnological Inventions.

48 Thomas R. Ilosvay, *Scientific Property,* 2 THE AMERICAN JOURNAL OF COMPARATIVE LAW 178 (1953).

country where, not only a human-made micro-organism was deemed patentable49, but also where the discovery of a function pertaining to a 'product of nature' like genes or DNA sequences was considered a human invention. Hence, the matter is no more how inserting a new type of right along the scientific research chain. On the contrary, the abstract objects conceived by scientists are directly considered as patentable subject-matter and the question has transformed into where to draw the line between mere discoveries and inventions.

Thus, the US decided to act as main defender of these patenting practices in biomedical research, also in the light of certain property claims expressed by all the involved national industries. In fact, these corporate innovators started demanding more proprietary protection from the federal government given that, on one hand, biotechnology is effectively a high-cost and high-risk activity but, at the same time, because patents, as anticipated by Hegel a long time ago, are a powerful tool for proprietary control over intangibles50.

Even so, current propensity to grant patents on genes or research tools is a fuzzy theme anyway, thence the reasons behind innovators' need to cry out for this kind of protection have to be accurately searched

49 Sidney A. Diamond, Commissioner of Patents and Trademarks v. Ananda M. Chakrabarty, et al., 447 U.S. 303 (1980).
50 DRAHOS, A PHILOSOPHY, *supra* note 14, at 83-85.

out. Basically, patents are just one of the many potential legal instruments issuable in order to spur innovation, thereby any applicant should consider them as the best existing incentive when he decides to rely on them, although he has never done before. There is a multitude of reasons behind a change of attitude toward patenting, with both endogenous and exogenous origin, at least in biomedicine.

First, the "linear model" of scientific innovation that Vannevar Bush designed in 1945 is no longer valid, so much that nowadays we refer to science as an innovation "cycle". In fact, an ever growing part of basic science is already motivated by practical application rather than being curiosity-driven, as tradition would have it. Furthermore, evidence demonstrates the deep interaction between basic and applied scientific technologies51, insomuch as it has been coined the new, more proper, distinction from upstream and downstream research, as a substitute of the traditional basic and applied research dichotomy. As a consequence, the separation between non-patentable discoveries, one time typical output of basic science, and inventions, industrial applicable products of applied research, has turned into something objectively difficult to delineate, and so it has also become easier to reach instrumental

51 Richard R. Nelson, *The Market Economy and the Scientific Commons* 17, 26-28, in INTELLECTUAL PROPERTY RIGHTS: INNOVATION, GOVERNANCE AND THE INSTITUTIONAL ENVIRONMENT (Birgitte Andersen ed., Edward Elgar Publishing, Cheltenham-Northampton, 2006).

characterization of works of nature as novel human-made invention52.

However, that may be still not enough to explain why innovators have suggested their governments to consider upstream biological innovation as patentable subject matter too. The combination between this circular model of innovation with blurred boundaries between basic and applied research, and the high cost of long and expensive routes leading to scientific knowledge, is somehow the most frequent explanation. In the context of such innovation cycle, heterogenous actors contribute to research activities and bear related R&D costs. Since all these contributors, including pharmaceutical firms, biotechnology startups, universities and governments, from the upstream to the downstream level, have developed an inclination towards patenting, a patent proliferation phenomenon is intervened in life sciences.

Moreover, if it is true that "every industry requires a unique form of patent protection"53, there should be as many patent theories about the role of patents, their optimal division between initial inventors and improvers, and their scope, as operating industries. It would derive that, in any case, anyone who is within the biomedical R&D cycle (both private and public, academic or corporate actors) looks for the specific function

52 Novelty, inventive step and industrial application are the patentability requirements generally present in national patent systems and evolved into international minimum standard of patent protection thanks to Article 27(1) of the TRIPS Agreement.
53 Burk and Lemley, *supra* note 45, at 1595.

provided by patents in that specific industrial sector.

Innovation in biotechnology is cumulative and complementary, which means that any final product collects together an original invention and subsequent improvements made by follow-on inventors, and it is the combination of two o more components into an integrated "structure"54. These features imply that property is fragmented into all the different subjects participating at the innovation cycle and, in order to be integrated for coming to the end product, has to be aggregated. The aggregation process may result in high search and transaction costs for obtaining all the necessary licenses. In any case, each patent does not protect an entire invention, but just one of those components constituting the final product, and so it cannot give exclusive rights to control all that product55. Patents transform themselves into licensing tools whose value depends on how much protection that patent gives in respect to the final

54 This term has been here expressly formulated in order to differentiate this integration process from the 'systems competition' model pertaining to the digital technology field. Whereas this model has complementarity aspects like biotechnology, the distinguishing element is that pieces of each product must be made compatible by some kind of interface, as, for instance, occurs for computer operating system and compatible software: *see* Peter Menell and Suzanne Scotchmer, *Intellectual Property, in* 2 HANDBOOK OF LAW AND ECONOMICS 1526-28 (A. Mitchell Polinsky and Steven Shavell eds., Elsevier Science Publishing, Amsterdam, 2007). However, interoperability may be relevant for bioscience too. The frontiers of science are moving from biological engineering, or else biotechnology, to biological programming, thanks to a new field called 'synthetic biology' which envisions the *de novo* design and programming of genes and organisms. Synthetic biologists consider the gene as algorithm which can be programmed like computers, hence any developed DNA sequence should comply with technical standards to ensure interoperability with all the others: *see* Andrew W. Torrance, *Synthesizing Law for Synthetic Biology,* 11 MINNESOTA JOURNAL OF LAW, SCIENCE AND TECHNOLOGY 629, 635, 636, 659 (2010).

55 Menell and Scotchmer, *supra* note 54*,* at 1591, 1595, 1610-1612.

product and how much bargaining power that patent gives within the aggregation process.

Such distinguishing problem which may arise within the biomedical innovation process, namely the high number of patent holders as determinant of potential costly negotiations and holdouts problems56, also fits well into the canonical definition of "anticommons" coined by Michael Heller57.

At first glance, it might appear somehow counterintuitive that a fragmented ownership of innovation could determine an underuse of knowledge as a consequence of the right of any holder to exclude others, especially if we consider the traditional economical literature on cumulative innovation. According to these leading economists, follow-on innovators deserve patent rights since they also need incentives to innovate, and a balance of protection between them and the pioneer inventor is desirable and more pro-competitive than a monolithic

56 In patent law, holdouts are who refuse to license their patent unless paid to do so: *see* Rochelle Cooper Dreyfuss, *Varying the Course in Patenting Genetical Material: A Counter-Proposal to Richard Epstein's Steady Course,* 50 ADVANCES IN GENETICS 195 (2003).

57 The concept of "anticommons" mirrors the image of commons property. Making reference to the term "tragedy of commons" coined by Garrett Hardin in 1968 and deepened in the Nineties by Elinor Ostrom, Heller introduced the idea of the "tragedy of anticommons". This last situation occurs when too many owners have the right to exclude the others but no one has an effective privilege of use, and so a problem of underuse of scarce resources may emerge: *see* Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Market,* 111 HARVARD LAW REVIEW 621 (1998).

ownership58. Then, why is such theory of "tailored incentives" expressed by Nelson and Merger not immediately applicable to biotechnology industry?59 Or else, why in this field a fear of a "tragedy of anticommons" emerges instead of rival and efficient contributions to innovation?

The necessary antecedent for answering the first question has been already outlined and, more precisely, is represented by the additional element of complementarity into cumulative research. When contributors owns complementary abstract objects, rivalry between innovators is not desirable since it may lead to non-cooperative behaviors, making the aggregation impossible o extremely difficult to reach60.

At this point, in the light of such peculiar features of biomedical research, we would imagine a completely different patent landscape around this innovative field. Since cooperative efforts are required for coming to aggregation, for which reason all these heterogenous actors in

58 *See,* e.g., John H. Barton, *Patents and Antitrust: A Rethinking in Light of Patent Breadth and Sequential Innovation,* 65 ANTITRUST LAW JOURNAL 449 (1996-1997); Jerry R. Green and Suzanne Scotchmer, *On the Division of Profit in Sequential Innovation,* 26 RAND JORNAL OF ECONOMICS 20 (1995).

59 Robert P. Merges and Richard R. Nelson, *On the Complex Economics of Patent Scope,* 90 COLUMBIA LAW REVIEW 839 (1990) where is stated that the economic significance of a patents depends on its scope. With regard to licenses, they admit a defect of the one-size-fits-all patent regime in not being able to distinguish cases where blocking rights are not necessary for covering costs from cases where the original inventors would not invest without a profit from licensing.

60 Such danger may origin from either earlier inventor or rivals and it is caused by the worry that improved products enter the market. As for the former case, *see* Merges and Nelson, supra note 59, at 841; as for the latter one, *see* Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law,* 5 JOURNAL OF ECONOMIC PERSPECTIVES 29 (1991).

biomedicine rush and push for patenting?61 It would be understandable if, at least for complementary innovative elements, private property was left aside: as said, each patent would be just used as a licensing tool and, more than the cost of patenting, long and expensive negotiations for orchestrating the overall transactional aspect are required62.

Nevertheless, reality is pretty different. A general tendency for private, instead of public, domains, in biotechnology is demonstrated by the high number of patents. Anyhow, assuming that innovators are rational economic actors, there should be one or more reasons capable to explain the enduring proprietary inclination.

Patents in biomedicine might still work as incentives to innovate because permanent valuable tools for recouping the high costs and for sustaining the high risks of biotechnology research. Actually, the classic incentive-to-create theory still partially describes the grant of patents to pharmaceutical companies, though the Kitch's prospect theory appears

61 In the Eighties 'patent races' received attention from a large part of the economics literature which evaluated the factors determining how many innovators would enter a race, the degree of competition or where shake-out point is placed. In this connection, it is worth recalling that one of the defects of patent law as an incentive mechanism is that investments it spurs might not be efficient since the private value for entering a race is different from the social value. Moreover, the patent race implies a imperfect sharing of information between firms about cost efficiency and the value of investments: *see* Menell and Scotchmer, *supra* note 54, at 1526-27.

62 Transaction costs have three main elements, namely the cost of searching for licensees or licensors, the cost of negotiation, and the cost of enforcing the license terms and protecting against non-licensees: *see* Clarisa Long, *Proprietary Rights and Why Initial Allocations Matter,* 49 EMORY LAW JOURNAL 823, 827-831 (2000).

appropriate too63.

According to this last theory, the benefit of a patent does not lie as much in its *ex-ante* incentive to create, but rather in the *ex-post* incentive to make investments on further ideas and for securing them from competitors appropriation, as well as to commercialize in a way that duplicative research is avoided and information exchanged64. Within the prospect theory, a patent gives its owner an *ex-post* right to control his invention in the market. In this way, the role of the single owner is emphasized since he is in a position to coordinate the development and improvement of his invention65. Then, it is worthwhile to understand

63 Legal and philosophical attention has recently focused on the incentive argument for intellectual property, or better whether the exclusive right to use and control information goods is necessary to spur creative production. In this connection, it is worth noting the difference between those cases in which exclusivity works as a motivation for creation and those cases in which exclusivity facilitates the creation, thanks to some funding and control over the work during creation: *see* Seana Valentine Shiffrin, *The Incentives Argument for Intellectual Property, in* INTELLECTUAL PROPERTY AND SOCIAL JUSTICE, *supra* note 1, at 94, 96. In regard to this examination of patent functions, only the incentive-to-create theory pertains to the former while all the others fit in the latter case since control and funding are facilitators of the invention but their prospect is not the aim of the innovative production. That raises the question whether patent protection is the only way to ease innovation in circumstances of the latter kind, and whether strong patent rights are preferable to weak ones. *See also* Giovanni B. Ramello, *Intellectual Property, Social Justice and Economic Efficiency: Insights from Law and Economics* 1, in INTELLECTUAL PROPERTY LAW: ECONOMIC AND SOCIAL JUSTICE PERSPECTIVES (Anne Flanagan and Maria Lillà Montagnani eds., Edward Elgar Publishing, Cheltenham-Northampton, 2010).

64 Edmund W. Kitch, *The Nature and Function of the Patent System,* 20 JOURNAL OF LAW AND ECONOMICS 265, 275-280 (1977).

65 It is worth noting that after Kitch there have been developed modern ex post justifications to patents. Basically, the point of convergence of all these justifications is the incentive patents give to manage or control already created works. They have been criticized since based on an unproven tragedy of anticommons and depend on private ordering without relying on market ordering: *see* Mark L. Lemley, *Ex Ante versus Ex Post Justifications for Intellectual Property,* 71 The University of Chicago Law

whether there is anyone within the biotechnological innovation cycle who has such power of control and coordination, and whether he is actually keen to use it.

Above all, inside a cumulative research-based industry, broader is the scope of one patent in respect to the others, stronger is the power to control the overall inventive process. Complements, instead, arise a threat of overlapping patents when any patent is broader than the real knowledge good protected by itself, insomuch as they might cover the same ground and so create a so-called "patent thicket"66.

In case of basic equivalence of strength, a downright "tragedy of anticommons" may occur when inventors underuse patented knowledge because of the reciprocal obstacles that their patents pose. Moreover, anticommons elements are able to worsen the problem of blocking patents, that is patents which cannot be invented around since covering essential features of the invention, without regard to their broadness. In sum, the allocation of inventors rights in biomedical R&D has not a unique, predefined formula, on the contrary it depends on these relevant and unpredictable factors67.

Review 129 (2004).

66 Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting* 2-5 (U.C. Berkeley, Competition Policy Center, 2001) available at http://escholarship.org/uc/item/4hs5s9wk (last visited August 5, 2010).

67 The organization of an innovative environment is able to affect the incentive to undertake R&D and, in reverse, the task of undertaking R&D may induce a re-

Apart from magnitude and allocation, inside the biomedical sector, the power of control, and so the value, pertaining to each patent is not linked to the overall invention anyway since, as said, there are other patent owners along the innovation chain. Thus, in this case, an efficient use of a patent should not lie in the enforcement of the right so as to exclude competitors, but rather in the assignment of patent rights68. On the contrary, patents typically give such exclusive right to exclude, or at least to decide who may be included in the use of any patented good. Along this line of reasoning, it may sound high questionable that filing a patent not devoted to these purposes still make sense. In truth, when patents are not able to reward, either past or future investments, they work as incentive to innovate if inventors attribute some merit besides those exclusionary capabilities, and innovation reality shows that these additional roles of patents actually exist.

Looking at the history of technology, for ages governments promoted the creation of technical and scientific knowledge by prizes and auxiliary

organization within that environment: *see* Menell and Scotchmer, *supra* note 54, at 1526.

68 *See* Article 28 of the TRIPS Agreement which states the right conferred to patentees: 1. A patent shall confer on its owner the following exclusive rights: (a) where the subject matter of a patent is a product, to prevent third parties not having the owner's consent from the acts of: making, using, offering for sale, selling, or importing for these purposes that product; (b) where the subject matter of a patent is a process, to prevent third parties not having the owner's consent from the act of using the process, and from the acts of: using, offering for sale, selling, or importing for these purposes at least the product obtained directly by that process. 2. Patent owners shall also have the right to assign, or transfer by succession, the patent and to conclude licensing contracts.

public awards, and so, patents cannot be considered strictly necessary for that end69. As a consequence, while it is true that patents do contribute to innovation, they are not the only tool to obtain it, and presumably their positive impact is not primarily related to rewards procured excluding competitors70.

Despite of the large, and growing, number of patents released within developed and emerging countries, many of them are just considered as 'missing patents' since not enforced or not maintained. For instance, in the US only 1 percent of issued patents are ever litigated71, and nearly two-thirds of all granted patents lapse for failure to pay maintenance fees72. In the context of 'missing patents' it is certainly relevant the age-old problem with regard to patent quality, that is to say, the issue of the scarce level of technical evaluation made by patent offices which later lead

69 Prizes are able to capture investments from unexpected sources, but not necessarily from the most efficient ones. In theory, this mechanism has the edge over patents when prize givers can base the prize on the value of innovation, but in practice this *ex ante* valuation is extremely difficult to assess. Further, with patents as a fallback option, an inventor would not accept a prize less than the patent value. On the other hand, grants overcome prize inconvenience of *ex post* rewarding, and so the need for the inventor to find funding to carry out his research, but they allow inventor to propose a research he cannot accomplish or, in any case, a waste of funds: *see* Menell and Scotchmer, *supra* note 54, at 1530-32.

70 NUNO PIRES DE CARVALHO, THE TRIPS REGIME OF PATENT RIGHTS 30-31 (Kluwer Law International, Alphen aan den Rijn, 3rd ed., 2010).

71 Mark A. Lemley, *Reconceiving Patents in the Age of Venture Capital,* 4 JOURNAL OF SMALL & EMERGING BUSINESS LAW 137, 142 (2000).

72 Mark A. Lemley, *Rational Ignorance at the Patent Office,* 95 NORTHWESTERN UNIVERSITY LAW REVIEW 1495, 1503 (2001).

courts to invalidate a large part of granted and then litigated patents73. Seeing that around half of all litigated patents are then declared invalid, included certain of conspicuous commercial value, a patent holder who alleges an infringement incurs the risk to lose his property right, therefore he might decide to refrain from litigating that patent at all74. However, a patentee may decide for not paying the maintenance fees just because his patent has arrived at the end of its 'effective life', namely when the protected innovation is supplanted by an improved version75. At any rate, even in case of enforced patents, the long waiting times for getting a legal result from any patent litigation suits makes unlikely that the main purpose of patent enforcement would lie in competitors exclusion, but rather in a mere economic compensation for any infringement76.

In sum, reality shows us that every year more and more patents are granted all over the world, most of them in the US, but a relevant amount also in Europe and within innovative developing countries (IDCs) like China and India. Many patents expire, very few are enforced and almost none of them for excluding competitors. Again, and always considering

73 John R. Allison & Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents,* 26 AIPLA QUARTERLY JOURNAL 185 (1998).

74 Mark A. Lemley and Carl Shapiro, *Probabilistic Patents,* 19 JOURNAL OF ECONOMIC PERSPECTIVES 75, 76 (2005).

75 In some industries 60% of the effective patent life terminate within four years: *see* Edwin Mansfield, *Patents and Innovation: An Empirical Study,* 32 MANAGEMENT SCIENCE 174 (1986).

76 Lemley, *Reconceiving Patents, supra* note 71, at 145.

patentees as economically rational actors, it is worth finding an explanation of their choice to file patents, and so to bear the cost of obtaining them, even in cases when they have small value or it is unlikely that the right to exclude will be exerted.

Indubitably, it is not an easy task to predict which patents will have economic significance, and sometimes patent applicants effectively fail to understand the value of patents77. A certain degree of uncertainty is inborn in all property rights, but when patent rights are affected by uncertainty impressive consequences on innovation and competition may spring out78.

The distribution of value is highly skew in technological innovation, with a small number of "spectacular"79 patents of conspicuous commercial importance. Often, even though innovators are really uncertain about the economic significance of their inventions, they patent

77 Uncertainty over the commercial viability of patents on basic research results may require the reliance on proxies to establish a value for that patent. However such proxies are often more driven by reputation matters rather than the real quality of the patented invention: *see* Long, *Proprietary Rights, supra* note 62.

78 Lemley and Shapiro, *supra* note at 54, 81.

79 The reference is to Schumpeter's characterization of technological innovation. He wrote that 'spectacular prizes much greater than would have been necessary to call forth the particular effort are thrown to a small minority of winners, thus propelling much more efficaciously than a more equal and more 'just' distribution would, the activity of that large majority of businessmen who receive in return very modest compensation or nothing or less than nothing, and yet do their utmost because they have the big prizes before eyes and overrate their chances of doing equally well': *see* JOSEPH A SCHUMPETER, CAPITALISM, SOCIALISM, AND DEMOCRACY as quoted in F. M. Scherer, *The Innovation Lottery, in* EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY 3, 3 (Rochelle Dreyfuss, Diane L Zimmermann, Harry First eds., Oxford University Press, New York, 2001).

them anyway, knowing that most of those patents will be worthless, but hoping that a few will pay off for others. In this sense, patents have been liken to lottery tickets, and, just like lotteries, the bigger becomes the prize, the more people flock to buy them. In other words, when promising areas of innovation appear, more patent applicants try to find ways to get the chance of gaining patent protection.

Moreover, generally patent owners want to improve such chances of winning and, for doing that, they add detrimental practices such as filing continuation application or pernicious related patent applications80.

In fact, often biotechnology and pharmaceuticals firms, after filing a patent application, and for the entire lifetime of the patent, continue prosecution of related applications so that, if the original patent becomes obsolete because of market changes, or invalid by any court ruling, they will be protected anyway. As a consequence, the function attributed to patent disclosure of encouraging competitors to invent around so as to develop new inventions is frustrated81. Since continuation applications concerning the first patent may cover what afterwards invented around by competitors, these follow-on innovators refrain from doing improvements and derivative inventions in order to avoid any infringement of the original

80 Lemley and Shapiro, *supra* note 74, at 81.

81 Therefore, the the positive contribution of patents to pro-competitive invent around practices since avoiding the re-creation of previous inventions is nullified, and so the higher value of patents compared to trade secrets: *cf.* NUNO PIRES DE CARVALHO, *supra* note 70, at 42-43.

patent. In addition, patent owners may decide to file multiple patents on closely related technology for improving their chance of winning in a promising innovative field. This means that many patents cover a single invention and then "patent tickets" may arise82.

Not only, considering that defensive patenting is more likely within industries affected by patent thickets, such practice increases even more thickets density and so the likelihood of anticommons83.

Defensive patenting is one of the main causes of patent proliferation in biomedicine. Often patent applicants look for patents just to protect themselves from other people who already have patents, in hopes of deterring these other players from suing them. Others get patents since they are afraid that competitors have them or in order to set a patent portfolio large enough to enter in cross-licensing deals. All these defensive uses of patents are frequent in high-technology and startup companies, in which contexts patent licenses become essential tools with remarkable peculiarities84. In these circumstances, moving away from the typical model of licensing for royalties, patentees put their efforts to build portfolios of hundreds of patents to gain bargaining power in licensing

82 Lemley and Shapiro, *supra* note 74, at 81.
83 *Id.,* at 82.
84 Lemley, *Rational Ignorance, supra* note 72, at 1504.

negotiations85, and it is quite common for companies with roughly equivalent portfolios to agree on favorable or even royalty-free terms86. Per contra, newcomers and small entities who do not have large portfolios may encounter serious obstacles to cross-license, and so they face a "royalty stacking" issue. In fact, when the exchange of patent positions is not viable, they should pay royalties to each one who holds a patent in that relevant technology and, again, anticommons problems may arise87.

Kitch's idea of patents as guarantees against free riding competitors, in view of the zero marginal cost of duplication for knowledge goods, although correct for explaining the perdurance of patenting even without the incentive for inventors to exclude all the competitors, reveals not complete. While patent rights may reduce such 'inappropriability' problem88, refraining third parties from copying the inventions in view of the legal consequences of patent infringement, a simpler, and maybe more effective, way to solve that issue would be an extended use of trade secrets. However, and making reference to the relationship between

85 Cross-licensing of sizable patent portfolios may represent an alternative also to high stakes patent litigation: *see* Menell and Scotchmer, *supra* note 54, at 1519-20.

86 Lemley, The Rational Ignorance, *supra* note 72, at 1505.

87 With reference to commercialization inefficiencies of patents: *see* Lemley and Shapiro, *supra* note 74, at 82, and John S. Leibovitz, *Inventing a Nonexclusive Patent System,* 111 THE YALE LAW JOURNAL 2251, 2262-2263 (2002).

88 The optimal allocation of resources for the creation of inventions is inhibited by several problem identified by Kenneth Arrow in terms of inappropriability, indivisibility and uncertainty. *See* Kenneth J. Arrow, *Economic Welfare and the Allocation of Resources for Invention*, in SCIENCE BOUGHT AND SOLD: ESSAYS IN THE ECONOMICS OF SCIENCE 165 (Philip Mirowski and Esther-Mirjam Sent eds., The Chicago University Press, Chicago-London, 2002).

patent rights and trade secrets, it has been maintained that the last one should be regarded as residual legal device89. Excepting cases which embrace public security matters, secrecy is less socially efficient, and patent disclosure solves and reduces transaction costs arising from the 'indivisibility' problem of information goods90. The importance of patents has been exactly found in their ability to reduce the transaction costs related to the lack of information about inventive activities91, given that patents help to quantify technology, and to describe its quality too, through specifications and claims. Then, such signaling function of patents, which leads to consider them as gauging devices to measure the value of inventions, in principle should be desirable for patentees and society too92.

As a matter of course, the economic relevance of inventions is determined by markets, and certainly not by officers at the time of the examination in case they are patented. Hence, patents are issued

89 Channeling doctrines assert that patent law is an antidote to the non-disclosure aspect of trade secret law and, for this purpose, inventors who rely upon trade secrets are penalized compared to patentees. Particularly, they incur the risk that a later inventor obtains a patent on what they hold as a secret and blocks the use of that invention: *see* Menell and Scotchmer, *supra* note 54, at 1511.

90 For an extended overview of this classical categorization of sub-optimal allocation of resources for information goods: *see* Arrow, *supra* note 88, at 165.

91 This line of reasoning seems to contradict the preceding analysis on the increase of transaction costs because of patent proliferation. On the contrary, we may conclude that patents have ambiguous effects on transaction costs since they are able to reduce information costs along some margins but they increase them along others: *see* Clarisa Long, *Patent Signals,* 69 THE UNIVERSITY OF CHICAGO LAW REVIEW 625, 664-679 (2002).

92 NUNO PIRES DE CARVALHO, *supra* note 70, at 42-43.

regardless the merit of their subject matter and the field of technology, they may be later exploited or not, as large as patentees would like but also limited by higher social goals93. As a consequence, patents are considered mechanism to privatize information, but also effective screening devices94 to publicize it too95. Disclosing the invention, all the potential new developers may value its technical, and so economic, relevance before paying for it and patentees are able to publicize that content without incurring in the risk of misappropriation. In this way, patent specifications facilitate the establishment of markets in technical knowledge but also permit to invent around when exclusivity creates barriers for the creation of new inventions96.

Sometimes, even more simply, patents are brought into play for shaping an idea registry, a record in which patentees number and qualify their prior art, or also as indicators of product differentiation, that is an instrument through which patent owners differentiate their products, and themselves, from anything else97.

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93 Even in 1942, the US Supreme Court ruled that 'the promotion of the progress in science and the useful arts is the "main object"; reward of inventors is secondary and merely a means to that end. In *United States v. Masonite Corp.,* 316 U.S. 265 (1942).

94 Menell and Scotchmer, supra note 54, 1476-77.

95 Long, *Patent Signals, supra* note 91, at 627.

96 In other words, patent disclosure has pro-competitive effects since it permits to develop new inventions without the risk of redundant research activities: *see* NUNO PIRES DE CARVALHO, *supra* note 70, at 42. However, this viewpoint does not consider the risk of anticommons when R&D is cumulative and complementary in which case working solutions like inventing around are more difficult to undertake.

97 Lemley, *Reconceiving Patents, supra* note 71, at 144.

In fact, patent are not only signals for the respective inventions but for their owners as well. Wideness and characters of a patent portfolio are easily measurable attributes which generally are positively correlated with other less easily measurable attributes such as knowledge capital. Therefore, intangible goods developers decide to build patent portfolios, to signal information about themselves that would be more expensive to convey through other means98, and which are particularly crucial when patents are used as financing tools. The positive correlation between the amount of venture capital activities and patenting propensity is evidence that patents are employed by holders in order to define their market model for their financiers, and the typical practice of patenting at a very early stage of the technology development process by entities involved in venture capital financing makes stronger this argument99.

All things considered, patent landscape in contemporary biomedical research appears truly patchy. Going even beyond arguments expressed by Burk and Lemley100, in the framework of a technology-neutral patent system, not only every sector molds technology protection in a unique form which considers its distinguishing innovation features, but also each actor operating in a same given industry looks for different patent

98 Long, *Patent Signals, supra* note 91, at 628.
99 See Lemley, *Reconceiving Patents,* supra note 71, at 143-144.
100 *See infra* p. 35.

protection effects.

Biotechnology startups, and universities too, surely take advantage of the defensive use of patents, in order to discourage competitors suits and to encourage cross-licensing deals with them. Frequently such actors also use patents to reduce information asymmetries between them and their observers. By means of patents they signal their own quality and they measure the value of most promising inventions, and so, patents act as gauging devices and financial tools at the same time. Typically biotechnology firms have venture capital as financial point of reference, while universities have external, often public, grants. However, interconnections between these two actors are multiple so that they reflect on the sources of financing too. Often universities give origin to startups and biotechnological enterprises have ramifications into academic laboratories. In this framework, strong links between public and private interests are especially evident and reinforced by the frequent patent transactions between these firms and the academic sector.

On the contrary, within the pharmaceutical sector, the value of a patent is still mainly framed in classical exclusivity terms and by the rents that patent enables the patent holders to capture. However, also in this field the R&D scenario is changing, and is multi-faced too. As a consequence of the increasing amount of partnerships and licensing

arrangements with the biotechnology sector as well as universities, pharmaceuticals are more and more virtual companies conducting in-house management of outsourced activities101. Since these R&D networks of suppliers will need to trade their patents to pharmaceutical enterprises, considerations related to the fragmentation and proliferation are relevant in this area too.

101For a more extended explanation about the so-defined "quiet revolution" of the pharmaceutical industry, that is outsourcing in drugs R&D, see Bill Love, *Virtual Pharmaceutical R&D: A Strategy for the Millennium?,* 1 PHARMACEUTICAL SCIENCE & TECHNOLOGY TODAY 89 (1998); David Cavalla, *The Extended Pharmaceutical Enterprise,* 8 DRUG DISCOVERY TODAY 267 (2003); David E. Clark and Christopher G. Newton, *Outsourcing Lead Optimisation: The Quiet Revolution,* 9 DRUG DISCOVERY TODAY 492 (2004), David Cavalla, *A Quiet Revolution in Lead Optimisation Services?,* 9 DRUG DISCOVERY TODAY 635 (2004), Roger Crossley, *The Quiet Revolution: Outsourcing in Pharma,* 9 DRUG DISCOVERY TODAY 694 (2004).

CHAPTER II

BIOMEDICAL PATENTING IN PRACTICE: INHERENT AND EMERGING TRADEOFFS (AND DISTORTIONS)

II.1) NORMS OF SCIENCE MODULATION THROUGH PROPRIETARY CLAIMS: THE REACH OF PATENT RIGHTS FROM DOWNSTREAM TO UPSTREAM RESEARCH

Biomedical R&D is performed thanks to the contributions of both public and private actors, but typically each of two sides with truly different roles and goals. While private enterprises invested for developing and improving applied inventions, public research organizations, and mainly universities, pursued basic scientific research and its wide dissemination into the public domain. However, academic research has been deprived from this traditional mission when governments asked universities to come out from their "ivory towers" and facilitate the commercial application of the fruits of innovative activity102. In order to expand technology transfer from upstream to downstream research, as well as collaborations between public and private sectors, proprietary protection, that is patents, has been extended from end-products to basic

102 Most notably, intellectual property rewards have been considered essential in order to diffuse academic biomedical discoveries beyond the research community: *see* Nathan Rosenberg and Richard R. Nelson, *American Universities and Technical Advance in Industry,* 23 RESEARCH POLICY 323 (1994).

research outputs, and the long-established "open science" model has no longer prevailed[103].

The *open science* model was identified by the sociologist Robert Merton taking as a central pillar the role of social norms among scientists for pursuing discoveries. With special attention to the basic research, he shaped the CUDOS principles, an acronym identifying four interrelated norms of the scientific community, namely universalism, communalism, disinterestedness and organized skepticism. According to Merton's theory of scientific norms, there is a norm of common ownership (i.e. communalism) of research results developed by all the community of scientists, regardless of race, nationality, or gender (universalism). Scientists must express these results without any interference from person beliefs (disinterestedness) and expose them to the critical scrutiny (organized skepticism)104. Some years later Michael Polanyi, a physical chemist turned philosopher of science, drew on the *open science* model for describing the scientific community as a group of people working on a jigsaw puzzle who cooperate by 'putting the puzzle together in sight of the others so that every time a piece is fitted in by one helper, all the others

103 For an historical overview on public patent policy and the traditional diverging interests of universities and innovative firms, *see* Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research,* 82 VIRGINIA LAW REVIEW 1663 (1996).

104 ROBERT K. MERTON, *The Normative Structure of Science, in* THE SOCIOLOGY OF SCIENCES (H. Nowotny and K. Tascher eds., Edward Elgar Publishing, 1996) (1942).

will immediately watch out for the next step that becomes possible in consequence'105.

However, in the 1970s began the sociology of scientific knowledge (SKK) tradition whose representatives reported doubts and failures in describing science as a social activity. Thus, this constructivist view of science suggested that private ownership of scientific results is not necessarily malign nor benign since it mostly depends on the specific access practices in the relevant area106.

In this sense, emblematic of current patenting and licensing practices in biomedical science, and of the adverse impact on access to scientific knowledge, for both research and clinical use, is the *Myriad* case. Myriad Genetics, Inc. (hereinafter, Myriad) was founded in 1991 as a gene discovery company by Mark Skolnick (Adjunct Professor in the Department of Medical Informatics at the University of Utah, and Chief Scientific Officer of Myriad), Walter Gilbert (Nobel Laureate in chemistry, Professor in the Department of Molecular and Cellular Biology at Harvard University, and Vice Chairman of the Board of Myriad) and Peter Meldrum (past President and CEO of a company called Agridyne, and current

105 Michael Polanyi, *The Republic of Science: Its Political and Economic Theory* 465, *in* SCIENCE BOUGHT AND SOLD: ESSAYS IN THE ECONOMICS OF SCIENCE, supra note 88.

106 *see* JANET HOPE, BIOBAZAAR: THE OPEN SOURCE REVOLUTION AND BIOTECHNOLOGY 74-78 (Harvard University Press, Cambridge, 2008)

President and CEO of Myriad)107. Although since the early days Myriad has aimed to expand its activities to different fields like proteomics and drug development, its core business is on diagnostic testing for genes which predispose individuals to major disorders such as cancer and heart disease. The for-profit attitude of this Utah-based firm was manifest since the beginning108 but it becomes unequivocal with patents covering BCRA1 and BCRA2 breast and ovarian cancer genes.

In 1990, Mary Claire-King, a geneticist at the University of California, Berkeley, mapped the position of the gene BRCA1 in which germ line mutations engender a predisposition for breast and ovarian cancer. In August 1994, Myriad sequenced BCRA1 thanks to a ponderous computer database developed from to the extensive genealogical resources of the Mormon Church and the Utah Cancer Registry109.

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107 Initial start-up capital and funds to purchase necessary equipment came from a private stock offering that raised US$10 million, of which $1 million was equity from the Big Pharma company Eli Lilly. Moreover, Eli Lilly directly contributed to research on BRCA1 with another $1.8 million over three years in return for licensing privileges: see Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing,* 10 HEALTH LAW JOURNAL 123, 129 (2002).

108 A Myriad's press release of April 1994 stated: 'Myriad is establishing a genetic information business based on testing for genes which predispose individuals to major common diseases. The genetic information business represents a multi-billion dollar market opportunity for the Company just for testing of individuals affected with disease and their family members. As genetic disease testing moves toward a general population screen, the market size increases dramatically': *see* KEVIN DAVIES AND MICHAEL WHITE, BREAKTHROUGH: THE QUEST TO ISOLATE THE GENE FOR HEREDITARY BREAST CANCER 223 (Macmillan Books, London, 1995)

109 From a global distributive justice perspective, genetics has a strong potential for improving global health but in practice much depends on how benefits arising from this scientific field are actually distributed. In general the patent system, as it

Immediately, an issue arose with regard to the patent application. Despite this breakthrough was attained with the contribution of other researchers, among which two colleagues working at the NIH (US National Institutes of Health), Myriad did not include their names as co-inventors in order to avoid any sort of obstacle with the exercise of exclusive rights110. While a following settlement which led to add such names to the patent application seemed to solve all the problems in the US, a real European rebellion came after with a number of oppositions at the EPO (European Patent Office) against patents granted to Myriad for genetic testing related to BRCA1111.

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functions now, is not compatible with a distributive justice framework since it would need to support more access to health and to consider every individual, not just the patent owners, as 'units of moral concern': *see* LOUISE BERNIER, JUSTICE IN GENETICS: INTELLECTUAL PROPERTY AND HUMAN RIGHTS FROM A COSMOPOLITAN LIBERAL PERSPECTIVE 116-145 (Edward Elgar Publishing, Cheltenham-Northampton, 2010). This reasoning should gain strength in the light of Myriad's patents on BCRA1 since the private appropriation of human genetic resources, and so the commercialization of relevant genetic technology, was possible thanks to population databases. This last aspect raises even more legal and ethical issue with regard to the relationship between commercial interest and scientific research as well as the role of intellectual property. For this purpose, *see* Jennifer French, *Something is Rotten in the State of Iceland: deCODE Genetics, Population Research and Informed Consent*, *in* PATENT LAW AND BIOLOGICAL INVENTIONS 113 (Matthew Rimmer ed., The Federation Press, Leichhardt, 2006) about the earliest, and most controversial, population databases. In 1998, Icelandic government granted deCODE Genetics Inc an exclusive license to access the country's medical records.

110 More precisely, the sequence of BRCA1 was achieved with help from researchers at the University of Utah, McGill University and NIH. It is worth noting that Myriad was assisted by government agencies like the NIH not only through the provision of their researchers but also with more than $5 million funding: *see* Williams-Jones, *supra* note 107, at 131.

111 After *The Institut Curie v. Myriad Genetics Inc.,* European Patent Office Opposition Division (3 November 2004) against European Patent EP0699754, Myriad quietly dispossessed itself of the ownership of that patent and assigned it to the University of Utah Research Foundation as a consequence of the Opposition Division decision.

In 1996, Myriad filed a patent application for the 'Chromosome 13-linked breast cancer susceptibility gene BRCA2' in spite of all the efforts of Professor Michael Stratton to avoid the commercial exploitation of that discovery. Stratton, who led a consortium of UK researchers at the Institute of Cancer Research and the Sanger Centre, located that gene with the collaboration of Skolnick. After the move of Myriad, or rather, of its co-founder Skolnick, for patenting BRCA1, Stratton decided to publish, so as to destroy novelty, the research results and, in the meantime, to hide them from his American collaborators. However, Skolnick was able to obtain enough information and filed the patent. Stratton reacted with defensive patents covering some gene mutations, but the one of Myriad had a broader scope, precisely the whole gene112. The EPO issued that patent in 2003 and a joint opposition at the EPO from the Belgian Society

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In fact, although the EPO rejected some arguments argued by the *Institut Curie,* it held that the patent application failed to comply with Article 56 of the European Patent Convention 1973 which requires an inventive step. Myriad declared that it was just 'another step in a long administrative review process' but the New York Times reported that Myriad stock dropped 1.7 per cent after that decision. Later on, another opposition procedures were filed at the EPO against other Myriad's BRCA1-related patents: in *Sozialdemokratische Partei der Schweiz and the Institut Curie v. The University of Utah Research Foundation,* European Patent Office Opposition Division (19 September 2005) against European Patent EP705902; *The Institut Curie v. The University of Utah Research Foundation,* European Patent Office Opposition Division (9 June 2005) against European Patent EP705903.

112 Patents were also filed by OncorMed Inc, an another gene discovery company. Both OncorMed and Myriad sued for patent infringement but Myriad settled out of court purchasing OncorMed patents for an undisclosed fee: *see* Williams-Jones, *supra* note 107, at 132-133.

of Human Genetics and the *Institut Curie* followed113.

This case shows in practice, and with remarkable intensity, the concerns for patenting in genetics. This phenomenon has started from the US but it has far-reaching implications. The scientific community, using Merton's wording, is universal, but nowadays it is also integrated into a worldwide network, which means that it is globalized too. Scientists may work together on common projects while remaining in their own laboratories placed in different jurisdictions. Patenting approach of even only one contributor to any project has doubtless practical effects on the others wherever they are located. Myriad, or another entity on its behalf such as the University of Utah Research Foundation, has adopted very restrictive licensing practices for its blocking patents114, i.e. patents which, covering gene functions, cannot be invented around115. This

113 EPO upheld the patent in an amended form and narrowed the claim so as to cover only one particular mutation 'for diagnosing a predisposition to breast cancer in Ashkenazi Jewish women'. The term 'Ashkenazi' refers to Jewish with European origin. Other than being a quite imprecise categorization for historic and scientific reasons, the opponents argued that the patent may cause an ethic discrimination against Ashkenazi Jewish women. In practice, clinics have to ask women whether they are Ashkenazi Jewish or not. If a woman is not, she can do a free test, otherwise she has to submit herself to Myriad test which it also means paying for the patent license or send her own samples to Myriad laboratories: *see* MATTHEW RIMMEL, INTELLECTUAL PROPERTY AND BIOTECHNOLOGY: BIOLOGICAL INVENTIONS 199 (Edward Elgar Publishing, Cheltenham-Northamption, 2008).

114 Groups like Breast Cancer Action also criticized Myriad for its public education program arguing that it was more focused to convince women and their physicians of the need for testing rather than to inform of the facts about breast cancer: *see* http://bcaction.org/index.php?page=newsletter-67a (last visited January 24, 2011).

115 Geertrui Van Overwalle, *Of Thickets, Blocks and Gaps*, *in* GENE PATENTS AND COLLABORATIVE LICENSING MODELS 383, 389-391 (Geertrui Van Overwalle ed., Cambridge University Press, Cambridge, 2009).

choice was unsuccessfully obstructed by Professor Stratton but later it faced a strong opposition from other European geneticists who have both ignored patents, so continuing to practice different BRCA tests, and formally objected Myriad's patents at the EPO. On the other hand, American geneticists' reactions were not so robust, in part because the United States Patent and Trademark Office (USPTO) does not allow a similar opposing procedure, but an another reason might be the already too tight linkage between corporations and academia, as exemplified by Myriad case itself. This case shows how transnational personal and communicative relationships influence and are influenced by international and national practices, norms and values116.

All in all, later the Myriad case has become the mirror image of the *Harvard OncoMouse* case. Whereas in the latter the US attitude towards biological organism patenting influenced Europe, the opposition proceedings against the European patents of Myriad opened the door for a lawsuit, and a landmark decision, against Myriad in the US. In fact, on May 12, 2009, the ACLU (American Civil Liberties Union Foundation) and the Public Patent Foundation filed a lawsuit on behalf of the Association for Molecular Pathology (together with eight researchers and genetic

116 For an extended overview regarding this issue, *see* FROM TRANSNATIONAL RELATIONS TO TRANSNATIONAL LAWS: NORTHERN EUROPEAN LAWS AT THE CROSSROAD (Anne Hellum, Shaheen Sardar Ali and Anne Griffiths eds., Ashgate Publishing, Farnham, 2010).

counselors, six patients, two women's health groups and four scientific associations) against BRCA1 and BRCA2 patents117. They sued the USPTO, Myriad Genetics and the University of Utah Research Foundation to declare invalid fifteen claims contained in seven patents for the BRCA1 and BRCA2 genes. Basing on Section 101 of the Patent Act118, but also on Article I, Section 8, Clause 8 of the US Constitution119 as well as the First120 and Fourteenth121 Amendments, plaintiffs challenged the validity

117 In *Association for Molecular Pathology, et al. v. United States Patent Trademark Office, et al.,* 09-CV-4515 US District Court for the Southern District of New York (2009).

118 Section 101 of Title 35, United States Code, provides that 'whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subjects to the conditions and requirements of this title'. The US Supreme Court in *Diamond v. Chakrabarty,* 447 U.S. 303, 308 (1980) held that 'the Congress plainly contemplated that the patent laws would be given wide scope' but, on the other side, the exclusion of scientific principles and *laws of nature* from patenting dates back to 1852 in *Leroy v. Tatham,* U.S. 155, 175 (1852). The Court in *Chakrabarty* basically held that *products of nature* may be patented but they must have 'markedly different characteristics from any found in nature'. However, in the recent *Lab. Corp. of Am. Holdings v. Metabolite,* 548 U.S. 124, 126-27 (2006), Justice Breyer recognized that 'the reason for this exclusion is that sometimes *too much* patent protection can impede rather than 'promote the Progress of Science and useful Arts' the constitutional objective of patent and copyright protection': *see* Motion for Summary Judgement filed by Association for Molecular Pathology et al, March 29, 2010 (Appeal from the US District Court for the Southern District of New York, in case no. 09-CV-4515, Senior Judge Robert W. Sweet).

119 According to Article I, Section 8 (Powers of Congress), [the Congress shall have the power] to promote the Progress of Science and Useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.

120 Amendment 1 (Freedom of Religion, Press, Expression) stipulates that 'the Congress shall make no law respecting an establishment of religion, or prohibiting the free exercise thereof; or abridging the freedom of speech, or of the press; or the right of people peaceably to assemble, and to petition the Government for a redress of grievances.

121 Clause 1 of Amendment 14 (Citizenship Rights) states that 'all persons born or naturalized in the United States, and subject to the jurisdiction thereof, are citizens of the United States and of the State wherein they reside. No State shall make or

of these patents claims since covering products of nature. On March 29, 2010, Judge Sweet made unsteady the lasting and strategic dependency on gene patents by biotechnology sector. In fact, in the light of 'long-recognized principles of molecular biology and genetics', he stated that these patents were 'improperly granted'. As maintained by the plaintiffs, their composition claims, i.e. the non-mutated and mutated isolated and purified forms of BRCA1 and BRCA2, have been regarded as 'laws of nature' while the method claims for detecting mutations, i.e. the comparison between mutated BRCA1 or BRCA2 with non-mutated ones, as mental processes, therefore unpatentable subject matters too. Even more clearly, he ruled that the argument that isolating a gene makes it patentable is a 'lawyer's trick' that 'circumvent the prohibition on the direct patenting of the DNA in our bodies but which, in practice, reaches the same result'122.

In sooth, long before biotechnology and genetics emerged, the US legal system upheld patents claiming natural products through the purification doctrine. In 1958, in *Merck & Co. v. Olin Mathieson Chemical Corp.* the Fourth Circuit upheld the validity of a patent claiming purified

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enforce any law which shall abridge the privileges or immunities of citizens of the United States; nor shall any State deprive any person of life, liberty or property, without due process of law; or deny to any person within its jurisdiction the equal protection of the laws.

122 Association for Molecular Pathology v. U.S. Patent and Trademark Office, No. 09 Civ. 4515, 2010 U.S. Dist. LEXIS 30629 at 4 (S.D.N.Y. March 29, 2010).

vitamin B-12 because of its therapeutic effectiveness and commercial value since 'there is nothing in the language of the [1952 Patent] Act which precludes the issuance of a patent upon a 'product of nature' when it is a 'new and useful composition of matter' and there is compliance with the specified conditions for patentability'. The court basically maintained that, to a certain extent, all products used to make inventions are from nature123. In 1991 the Federal Circuit approached the patentability of purified DNA in *Amgen, Inc. v. Chugai Pharmaceutical Co.* litigating the novelty and non-obviousness of a patent covering isolated and purified DNA sequences coding the production of human erythropoietin (EPO)124. Since the gene was isolated and purified, the Federal Circuit upheld the validity of Amgen's patent on DNA sequences. Later on courts have generally followed this reasoning, but the Supreme Court has never ruled on the purification doctrine, especially in the light of the 'markedly different characteristics' requirement identified in *Chakrabarty125.*

Any incoming ruling in *Association for Molecular Pathology* from the Federal Circuit, and perhaps the Supreme Court, will likely analyze this last aspect in depth. However that may be, courts are absolutely aware of the ponderous chain-reaction that any decision may bring, investing both

123 253 F.2d 156, 164 (4th Cir. 1958).
124 927 F.2d 1200 (Fed. Cir. 1991).
125 Ashley McHugh, *Invalidating Gene Patents: Association for Molecular Pathology v. U.S. Patent and Trademark Office,* 62 HASTINGS LAW JOURNAL 185, 193, 194 (2010).

the biotechnology industry and academia, but also their interdependence.

The Eighties may be considered a crucial decade in the transition toward the "privatization" of biological knowledge. In this context, the advent of genetic engineering and the resulting establishment of spin-offs biotechnology companies from academic laboratories126, the wide scope given to patents on genetically modified organisms, the multiplication of potential patent actors, including public-funded research organizations, are considered major factors of that change.

Furthermore, initiatives to overcome the territoriality principle of intellectual property (IP) rights have played another relevant role in innovation process. Since from the nineteenth century those countries considering themselves as net exporters of creative and technical knowledge have adopted international treaties to protect their IP owners outside national borders. While the initial bilateral treaties allowed IP holders only to claim the protection of their national laws into the other country, the subsequently multilateral agreements and the principle of national treatment have permitted treaties' advocates to export their IP models developed in order to support information creation127. Within

126 Biotechnology startups revenues have more than doubled between 1993 and 1999 (US$8 billion to US$20 billion) and tripled (to US$27.6 billion) by 2001. Their main, or only, resources are patents thanks to which they may raise initial capitals and funds: *see* Williams-Jones, *supra* note 107, at 126.

127 For an overview on these international influences, *see* LIONEL BENTLY AND BRAD SHERMAN, INTELLECTUAL PROPERTY LAW (Oxford University Press 3rd ed. 2009).

capitalistic societies, property rights, other than element of individual liberty, are considered powerful devices for promoting trade and markets as well as for obtaining efficient allocation of scarce resources and social welfare128. In order to cope with the globalization of information goods, Western private property culture, as applied to intangibles, has been gradually extended to other emerging markets129 determining a "direct geo-colonization" of intellectual property protection130.

Even though the impact of these national policies driven by "knowledge cartels"[131] started to be widely felt also earlier in third countries[132], since from 1995, several minimum standards coined by

128 Ramello, *supra* note 63, at 73-74.

129 So as to justify IP protection from a philosophical perspective, it would be necessary to evaluate western market paradigm and compare it with cultures pertaining to other societies: *see* Shiffrin, *supra* note 63. This kind of consideration, particularly useful in areas like traditional knowledge, requires to evaluate, for instance, the qualitative and quantitative merits of the different cultural outputs or the easiness to access to these output. Since these factors are very difficult to assess, this sort of evaluation has been simply ducked.

130 In earlier pages I argued that a "scope-colonization" together with an "indirect geo-colonization" occurred in the field of biomedical research. In that case, US practice of patenting genetically modified organisms influenced Europe through the claim, and the grant, of the Harvard Oncomouse patent which, in turn, led to the Biotechnology Directive approval. Here I refer to a "direct geo-colonization" since western countries, but especially the US government, were (and are) involved in unilateral and multilateral efforts in order to modify national rules of foreign countries for obtaining increased levels of IP protection: *see infra* at p. 33.

131 *See* Keith E. Maskus & Jerome H. Reichman, *The Globalization of Private Knowledge Goods and the Privatization of Global Public Goods, in* INTERNATIONAL PUBLIC GOODS AND TRANSFER OF TECHNOLOGY UNDER A GLOBALIZED INTELLECTUAL PROPERTY REGIME 18-19 (Keith E. Maskus and Jerome H. Reichman eds., Cambridge University Press, Cambridge, 2005).

132 BENTLY AND SHERMAN, *supra* note 127, at 5-8. In the Eighties, the US realized its innovative potential and, taking advantage of its trading power, threatened and imposed sanctions, by the means of Section 301 of the US Trade Act, against such countries not providing sufficient levels of patent protection. The American

western regulatory regimes, with a large part deriving from the U.S. patent system[133], are formally extending to all Members of the World Trade Organization (WTO), according to the grace period scheme allowed by the TRIPS Agreement. In particular, pursuant to Article 27 of the TRIPS Agreement, and provided that inventions meet the criteria of novelty, inventive step, and industrial application, gradually any WTO Member has to grant patents for any inventions, both products or processes, in all fields of technology[134].

Still in that period the nature of the US university as an institution with a public interest mission changed. The starting point brought back up to late-Seventies when the academic scientist Herbert Boyer, after having created the first genetically engineered organism, together with the venture capitalist Robert Swanson, founded the first biotechnology firm, Genentech. In August 1978, that firm announced the synthesis of human

unilateralism was reinforced by the lobbying activities of the pharmaceutical industry: Robert Weissman, *A Long Strange TRIPS: The Pharmaceutical Industry Drive to Harmonize Global Intellectual Rules and the Remaining WTO Legal Alternatives Available to Third World Countries,* 17 UNIVERSITY OF PENNSYLVANIA JOURNAL OF INTERNATIONAL ECONOMIC LAW 1069, 1075-77 (1996). In particular, the reform of 1988 established the so-called "Special 301" of the US Trade Act allowing USTR to impose sanctions on countries which did not have US-style patent law: *see* Wendy S. Vicente, *Questionable Victory for Coerced Argentine Patent Legislation,* 19 UNIVERSITY OF PENNSYLVANIA JOURNAL OF INTERNATIONAL ECONOMIC LAW 1101 (1998) (describing the case of Argentina).

133 *See* Eisenberg, *Public Research, supra* note 103, at 1663-1727 (describing the US government patent policy over the last years).

134 The European Council Directive 98/44/EC on the Legal Protection of Biotechnological Inventions, Article 1, actually specifies that this kind of inventions are patentable under the law of EU Member States if they satisfy patentability criteria, but national bodies can refuse patents on inventions that are contrary to *ordre public* or morality, a clarification not provided, for example, in the US patent system.

insulin, thus determining a terrific escalation of value in the Wall Street stock market, the rapid establishment of hundreds of other biotech companies, as well as the enactment of the Bayh-Dole Act (BDA) in the US.

The BDA of 1980 represented the expression of the 'revised social contract' between universities and the US government, authorizing the public funded recipients to patent their results and to decide their own licensing practices through dedicated technology transfer offices (TTOs), thus changing the presumption of ownership which until that moment favored the funding agencies[135]. Although it is often assumed that the BDA originated by the need to capitalize on the commercial exploitation of public-funded research, in reality the role of patents as a source of finance is marginal considering that, on average, half of all US universities has less than one million dollars income per year from royalties[136]. The main justification of patent rights as pecuniary incentive to create gives way to secondary arguments in support of patents, such as their transactional and signaling functions[137].

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135 Lisa L. Lieberwitz, *The Corporativization of Academic Research: Whose Interests are Served?,* 38 AKRON LAW REVIEW 759, 763-64 (2005).

136 Bart Verspagen, *University Research, Intellectual Property Rights and European Innovation Systems,* 20 JOURNAL OF ECONOMIC SURVEYS 607, 622-25 (2006).

137 For an overview on the role of patents in the biomedical sector, *see* COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH, WORLD HEALTH ORGANIZATION, *PUBLIC HEALTH, INNOVATION AND INTELLECTUAL PROPERTY RIGHTS* 32-35 (2006) [hereinafter CIPIH Report].

Whereas what is not owned cannot be exchanged in the market, what is patented becomes holder's private property and can be traded as a good or asset. The reliance on patents by US universities is mainly intended to collaborations with the industry by exclusive licenses[138], or directly for the establishment of spin-off companies from universities laboratories[139]. Moreover this new patenting approach has permitted to raise funding from strategic alliances with the pharmaceutical industry, such as the well-known 1998 Berkeley-Novartis agreement[140], and to signal innovative capabilities for measuring academic success[141].

The increase of US universities patenting became easier also by some judicial developments expanding the scope of patentability, and so proprietary trends for biological research, in which *Diamond v. Chakrabarty* case[142] represented the cornerstone, and the *Harvard Oncomouse* case the nodal point which reached also the European patent

138 *See, e.g.,* Mark A. Lemley, *Are Universities Patent Trolls?,* 18 FORDHAM INTELLECTUAL PROPERTY, MEDIA AND ENTERTAINMENT LAW JOURNAL 611 (2007-2008).

139 *See* CIPIH Report, *supra* note 137, at 37.

140 This kind of agreements, together with exclusive licenses of academic patented innovation, may have negative effects by facilitating corporations in the control of academic duties line. There is a conflict of interests, *i.e.* public interest against private economic interest, determining a decrease of inventions accessibility, a lack of independence of faculties, the tendency to market-driven research policies, an increased secrecy for preserving proprietary rights: s*ee* Lieberwitz, *supra* note 16, at 765.

141 Thomas J. Siepmann, *The Global Exportation of the U.S. Bayh-Dole Act,* 30 UNIVERSITY OF DAYTON LAW REVIEW 209, 219 (2004).

142 In 1980 the US Supreme Court ruled in favor of defendant Dr. Chakrabarty and confirmed that a genetically modified microorganism constitutes a patentable subject matters since 'a live, human-made micro-organism constitute a "manufacture" or "composition of matters"': Sidney A. Diamond, Commissioner of Patents and Trademarks v. Ananda M. Chakrabarty, et al., 447 U.S. 303 (1980).

system[143].

The privatization of public-funded research has raised criticism with reference to the use of public funding as an indirect subsidy to private businesses and for diverting the public interest goals of universities toward market-oriented research[144], but even more because the increase of university-owned patents is a fundamental element of the potential 'tragedy of the anticommons' in biomedicine.

In 1968 in *Science,* Garrett Hardin raised the problem of people's overuse of shared resources and introduced the metaphor 'tragedy of the *commons*' referring to that circumstances where too many owners have a 'privileges of use' and no one has 'rights of exclusion'[145]. Thirty years later Michael Heller and Rebecca Eisenberg, in the same journal, suggested an opposite type of problem, that is the 'tragedy of the *anticommons*', in which people underuse scarce resources because too many owners have a right to exclude each other but no one has an effective privilege of use[146]. Indeed, a fragmented ownership of complementary technology assets

143 In 1988 the USPO granted a patent on a mouse, genetically-modified to develop cancer by injecting an 'oncogene' and then the patentability of this invention was challenged in different countries. The European patent application was initially refused by the EPO but in the end, after a number of rulings, it was maintained on an amended form: (1989) OJ EPO 451 (Exam), T19/90 (1990) OJ EPO 490 (TBA), T19/90 (1991) EPOR 525 (Exam), (2003) OJ EPO 473 (Opposition Division). For a wider examination of the *Oncomouse* case, *see* BENTLY & SHERMAN, *supra* note 127, at 442-44.

144 *See* Lieberwitz, supra note 135, at 766.

145 Garrett Hardin, *The Tragedy of Commons,* 162 SCIENCE 1243 (1968).

146 Heller and Eisenberg, *supra* note 32.

requires coordination among the owners, and heightens the transaction costs associated with the transfer of those rights via licensing or other exchange mechanisms. Furthermore, the BDA gives universities the discretion to grant exclusive licenses of their patents to private companies, hence to limit subsequent works by others. In other words, these two academic lawyers highlighted and put a name to biologists fear of the ongoing proliferation of patent rights[147] in biomedical research and the potential detrimental effects on the progress of cumulative scientific research[148]. Insofar as the access to knowledge has always been considered as the essential element for cultural and scientific progress, in the past the existence of exclusive rights on academic inventions appeared counterintuitive, and nowadays, in spite of scientists departure from the Mertonian communitarian norms[149], appears really dangerous in the light of its potential negative effects on innovation development[150].

147 In the US, from 1985 to 2000, there was an explosion of the number of patents in biotechnology area. From 2,000 patents granted in 1985 to over 13,000 in 2000, growing by more than 600 percent: *see* John P. Walsh, Ashish Arora, & Wesley M. Cohen, *Effects of Research Tool Patents and Licensing on Biomedical Innovation, in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 293 (Wesley M. Cohen & Stephen A. Merrill eds., The National Academies Press, Washington D.C., 2003).

148 *See* Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine,* 66 LAW AND CONTEMPORARY PROBLEMS 289, 295-303 (2003).

149 Among others, crucial is the theorization of the norm of "communalism" by the sociologist Robert K. Merton implying the common ownership of research results ('The substantive findings of science are a product of social collaboration and are assigned to the community'): *see* JANET HOPE, BIOBAZAAR: THE OPEN SOURCE REVOLUTION AND BIOTECHNOLOGY 74-78 (Harvard University Press 2008) *citing* ROBERT K. MERTON, *The Normative Structure of Science, supra* note 104.

150 Whereas scientific community relies on the Isaac Newton's epigram "If I have seen

II.2) ACADEMIC PATENTING: UTILITARIAN OTHER THAN ETHICAL CONCERNS?

The departure from the traditional norms of science inside public research organizations, as a consequence of their role of patent owners, has raised criticisms and worries for potentially frustrating the public interest goals of academic freedom and dissemination of knowledge. Now, not only university's public interests overlap with private economic interests of innovative corporations, but the privatization of academic outputs is leading to a *corporativization* of universities, thereby determining a conflict of public and private interests within universities themselves.

Currently, universities seem to act as private firms in the way they license their patented research to the industry, gain faculty research support and faculty consulting fees, but in exchange they lose control of their results, sacrificing independence of faculty, admitting publication restrictions, and accepting limitations in sharing knowledge developed with public funding[151].

Nonetheless, concerns about the potential impact of commercial

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farther, it is by standing on the shoulders of giants", nowadays the use of prior discoveries in subsequent research is regulated by licenses, that is contractual arrangements, as a substitute of communal ownership: Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use,* 56 UNIVERSITY OF CHICAGO LAW REVIEW 1017, 1048-56 (1989).

151 *See* Lieberwitz, *supra* note 135.

incentives accorded to universities by patents have also a really practical perspective with respect to innovation enhancement. The strong rights conferred by patents provide patent owners the powers to define the "environmental conditions" of follow-on research. When thickets or blocks are so created, paradoxically, they may hinder instead of spurring biomedical research. Thus far, whether or not a 'tragedy of anticommons' has actually occurred remains a vexed empirical question, however obstacles in the patent landscape have already appeared.

The most frequently cited example is the aforementioned *Myriad* case, and the inherent adverse effects of gene patenting and licensing on access to diagnostic tests for mutation detection. However, other patents, covering different fundamental biological functions may have an even higher impact compared to that ones claiming DNA or genes functions. For the most part, universities own patents which do not involve commercial end-products (on the contrary, the peculiarity of genetic diagnostic tests is their dual use as both clinical and commercial products), but rather fundamental research tools. The term *research tool* generally refers to instruments, reagents, methods, and information 'the main commercial value of which is in furthering research'[152]. A survey of major US

152 Christopher M. Holman, *The Impact of Human Gene Patents on Innovation and Access: A Survey of Human Gene Patent Litigation,* 76 UMKC LAW REVIEW 295, 340 (2007-2008) *citing* NATIONAL ACADEMIES OF SCIENCE, BOARD ON SCIENCE, TECHNOLOGY, AND

universities, for example, showed that the medical school at Columbia University accounts for nearly 85 percent of all Columbia licensed patents, and more than 50 percent of them covers research tools[153]. As said, research tools broadly include all useful technologies for early-stage research which lead, step by step, to commercial end-products, hence patents on that inventions may quickly block subsequent innovation.

A clear example of research tool patents are the ones covering biological pathways, that is patents which claim various methods of treating human diseases based on the functionality of a pathway. A biological pathway is a group of cellular constituents wherein each constituent is influenced by one or more other cellular constituents in the group. In June 2002, Harvard University, MIT, and the Whitehead Institute obtained a patent on public-funded research on *NF-kB* cell signaling pathway and later they granted an exclusive license to the private company Ariad Pharmaceuticals (hereinafter, Ariad). Since NF-kB is a fundamental pathway involved in many diseases, from cancer and osteoporosis, to atherosclerosis and rheumatoid arthritis, this patent covers all drug treatments for all such diseases. As a consequence, now

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ECONOMIC POLITY (STEP), REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH 51 (Stephen Merrill & Anne-Marie Mazza eds., National Academic Press 2006).

153 *See* Annetine C. Geljins & Samuel O. Thier, *Medical Innovation and Institutional Interdependence: Rethinking University-Industry Connections,* 287 JAMA 72, 75 (2002).

Ariad is in the position to block development or commercialization of any drug that inhibit that pathway and, actually, that is what Ariad did soon after becoming the exclusive licensee of NF-kB patent. For instance, Evista and Xigris, two drug products marketed by the firm Eli Lilly, have infringed 20 claims of the Nf-kB patents which, in turn, lead to 65 million dollar award in favor of Ariad[154].

An another area of upstream research where patent blocks are likely to appear, and so the progress of follow-on activities to slow down, concerns stem cell lines. A prominent example refers to the broad claiming of the University of Wisconsin patent on primate embryonic stem cells. During the Nineties the American National Institute of Health (NIH) funded that university for deriving embryonic stem cells from rhesus monkeys and macaques, however the results were covered by a broader patent, claiming all primate embryonic stem cells. Moreover, later on, the same research team isolated human embryonic stem cells, but because of a moratorium on public funding for this research topic, the subsequent activities were funded by Geron, a private biotechnology enterprise, in exchange for exclusive rights on six types of differentiated cells that could

154 Shengfen Chen, *Pathways to Patents: Applying the Written Description Requirement Doctrine to Patents on Biological Pathways,* 30 HASTINGS COMMUNICATION AND ENTERTAINMENT LAW JOURNAL 559, 563-67 (2008).

be derived from human stem cells[155].

These cases clearly explain how the combination between broad patent scopes, and so claims, together with exclusive licensing practices of universities, and the cumulative character of upstream research in biotechnology, may really curb the actual amount of potential players in biomedical field, as long as restricts the access to essential research tools with wide applications in cumulative innovation.

Nevertheless, there is also some evidence that upstream patent rights may not only obstacle further basic research activities, but also applied developments. In particular, proprietary barriers, like blocking patents and higher transaction costs, have a peculiar dramatic impact on low commercial value research, such as for neglected tropical diseases[156].

The Global Forum for Health Research, within its report of 2003, underlined an allocative emergence for biopharmaceutical R&D, calling it the "10/90 Gap" because of 'only the ten percent of the world expenditure on health R&D is spent on health conditions that represent ninety percent of the global burden'[157]. Where private financial resources for drug development are already scarce, since market-based incentives behind

155 Rai and Eisenberg, *supra* note 148, at 293, 301.

156 Katherine M. Nolan-Stevaux, *Open Source Biology: A Means to Address the Access & Reseach Gaps?,* 23 SANTA CLARA COMPUTER & HIGH TECHNOLOGY LAW JOURNAL 271, 274-79 (2007).

157 GLOBAL FORUM FOR HEALTH RESEARCH, THE 10/90 REPORT ON HEALTH RESEARCH 2003-2004, *available at* http://www.globalforumhealth.org/ (last visited July 28, 2010).

patent system are not enough to stimulate innovation for not profitable markets, the current extended "commercialization" of academic research, with the highlighted transaction costs, may even sharpen global health disparities[158]. For instance, the PATH Malaria Vaccine Initiative (MVI), a program of the nonprofit organization PATH whose mission is to accelerate the development of malaria vaccines, reported complex patent nets surrounding each antigen relevant for malaria vaccines, as the 34 groups of patents claiming the antigen MSP-1[159].

Thus, these examples has permitted to show that patents may create barriers since the beginning until the end of the biomedical innovation pipeline, and how, in several cases, certain worries expressed in the recent past by scientific community have become reality. Looking at the current landscape of biomedical R&D, perhaps it is actually difficult to distinguish mere fears from oncoming dangers. The relevance of biotechnologies inside biomedical science is a fundamental element for understanding the lack of predictability and the co-existence of static and dynamic patent failures in this innovation field. Biotechnology is a new, cutting-edge technology that refuse to behave like traditional ones, hence

158 *See generally* Amy Kapczynski, Samantha Chaifetz, Zachary Katz & Yochai Benkler, *Addressing Global Health Inequities: An Open Licensing Approach for University Innovations,* 20 BERKELEY TECHNOLOGY LAW JOURNAL 1031 (2005).

159 MVI Patent Analysis *cited in* Arti K. Rai, *Proprietary Rights and Collective Action: The Case of Biotechnology Research with Low Commercial Value, in* INTERNATIONAL PUBLIC GOODS AND TRANSFER OF TECHNOLOGY UNDER A GLOBALIZED INTELLECTUAL PROPERTY REGIME, *supra* note 131, at 295.

old-fashioned solutions adopted in the past are not sufficient any more160.

In the framework of the patent law, and its inherent second-best solution of excludability for sustaining investments in technical information goods, some solutions are provided to face the typical trade-off between static costs and dynamic benefits, but not the dynamic problem of patent proliferation[161]. In fact, even though derogations from patent protection are even permitted by minimum standards setting of the TRIPS Agreement, they are expressly described as limited and subject to a number of conditions. Moreover, whereas, on one side, the right to invoke these so-called flexibilities was reaffirmed with specific reference to public health goals in the Doha "Declaration on the TRIPS agreement and Public Health"[162], on the other side WTO Dispute Settlement Body decisions have shown resistant to the admittance of exceptions to patent property rights and their exercise[163]. This is even more burdensome in the light of the entwined networks of regional and bilateral free trade agreements which

160 Maskus and Reichman, *supra* note 131, at 9.
161 *See id.*
162 Ministerial Declaration on the TRIPS Agreement and Public Health, WTO Doc. WT/MIN(01)/DEC/1 (Nov. 20, 2001).
163 Panel Report on *Canada – Patent Protection of Pharmaceutical Products*, WT/DS114/R (2000) and Appellate Body Report on *Canada – Term of Patent Protection,* WT/DS170/AB/R (2000): s*ee* Gail E. Evans, *Strategic Patent Licensing for Public Research Organizations: Deploying Restriction and Reservation Clauses to Promote Medical R&D in Developing Countries,* 34 AMERICAN JOURNAL OF LAW & MEDICINES 175, 183 (2008).

followed the origin of the WTO, that is the so-called "Spaghetti Bowl" phenomenon, and where the minimum standards of the TRIPS agreement are heightened by TRIPS-plus provisions[164].

Access to biomedical research is a natural premise for the access to health care. Besides problems posed by the globalization of the IP regime, the strong connection between commercial and non-commercial interests cause specific concerns, being this technological sector crucial for its economic potentialities, but also for producing health-related goods.

164 *See* Luis Abugattas Majluf, *Swimming in the Spaghetti Bowl: Challenges for Developing Countries under the "New Regionalism"* (UNCTAD Policy Issues in International Trade and Commodities Study Series No. 27, 2004).

II.3) The Unstable and Uneasy Use of Traditional Patent Law Flexibilities into Biomedical Arena

The commoditization of academic research has conveyed obstacles also in the use of the traditional patents safeguards, such as post-grant flexibilities.

A typical engine to mitigate the tension between public and private interests in the production of biomedical innovation is the scientific research exemption. According to the vague text of Article 30 of the TRIPS Agreement, WTO Members may provide limited exceptions to the exclusive right conferred by a patent when the public interest is superior to the private interest of the patent holder.

As said, in the biomedicine context is especially relevant the scientific research-experimental use exception since follow-on innovation often depends on patented know-how. The application of this exception permits therefore the access and use of the invention covered by proprietary rights without incurring in a patent infringement. On one hand, it is undoubted that this provision of the TRIPS Agreement works for acts done for purely scientific purposes, but, on the other hand, each Member has adopted a different approach to the undefined terms of

Article 30 as regards to those acts done for commercial purposes[165].

The US, in contrast with developing countries, but also other western legal systems, do not have a statutory defense for the experimental use of patented innovation. Historically the federal courts, and the Court of Appeal of the Federal Circuit (CAFC) later, have recognized a limited defense for the use of patented innovation for scientific purposes[166] and they have adopted a 'very narrow' interpretation when commercial activities were involved[167].

Nonetheless, the American research community has always, wrongfully, believed that educational institutions, such as universities, were fully protected by an experimental use exception to patent law. This is in part explained by the traditional use of an "informal" experimental use exception by academic researchers, that is an "ignore patents" norm, endorsed by the industry as well. Many reasons led to the adoption of an "ignoring infringement behavior" from companies, like the high cost of public reputation, detection and enforcement, but mostly because of the

165 The experimental use exception symbolizes a lasting diversity example in national patent laws in the post-TRIPS era: *see* John F. Duffy, *Harmony and Diversity in Global Patent Law,* 17 BERKELEY TECHNOLOGY LAW JOURNAL 685, 717-19 (2002).

166 Poppenhusen v. Falke, 19 F. Cas. 1048, 1049 (C.C.D.S.N.Y. 1861) (No. 11,279) in which the boundaries of the scientific research exception were conclusively defined, stating that 'an experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement [was] not an infringement of the rights of the patentee'.

167 Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools,* 76 WASHINGTON LAW REVIEW 1 (2001).

ties that bind them with universities[168]. However, this kind of solution remains imperfect because it is not enforceable under the law, keeping the follow-on innovators uncertain about the final outcome.

In addition, it is essential to underline that accessibility to IP in academic research has become even more limited as a consequence of the current private economic interests in academia's policies, in particular with reference to its patenting and licensing practices after the BDA. After the 2002 CAFC decision in the *Madey v. Duke University*[169] case, it is potentially precluded any unlicensed use of patents as the Court alleged that universities are, in effect, commercial entities that use research activities (and patenting) to compete for fund raising and prestige. As said, such uses were already illegal in the US system, however this decision calls the attention of the academia for potential future liabilities as a consequence of unauthorized uses of IP[170].

In sum, the workability of formal and informal research exceptions faces the difficulty of a blurred line between scientific and commercial experimentation because of the ever increasing commercial connections of the academic community[171], and this side-effect of the academic

168 *See* Cristina Weschler, *The Informal Experimental Use Exception: University Research after Madey v. Duke University,* 79 New York University Law Review 1536-1569 (2004).

169 In *Madey v. Duke University,* 307 F.3d 1351 (Fed. Cir. 2002).

170 Walsh et al., *supra* note 147, at 335.

171 EVANS MISATI & KIYOSHI ADACHI, THE RESEARCH AND EXPERIMENTATION EXCEPTIONS IN PATENT

privatization becomes far more acute given the absence of a shared approach for their scope among different national systems. At the same time, the dependence upon informal social norms of infringement leave ambiguity and raise skepticism considering its need of a close-knit homogenous community to operate. In particular, the changing nature of biomedical research and its tendency to attract members from other communities, such as information technology and nanotechnology, may transform "working solutions" as ignoring patents in unworkable ones[172].

Also the use of compulsory licenses to guarantee the freedom to access to essential patented technology, even if it can be considered as a possible remedy to the problem of blocking patents, brings some shortcomings. Since those licenses are exceptions to exclusive rights conferred by patents, strict procedures for their grant are set, both at international level by Article 31 TRIPS, and at national level by patent legislations. Therefore, the compliance with these legal constraints requires long and time-consuming operations, rendering this remedy an inappropriate tool to ensure day-to-day access and use to patented

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LAW: JURISDICTIONAL VARIATIONS AND THE WIPO DEVELOPMENT AGENDA 2-3 (UNCTAD-ICTSD Project on IPRs and Sustainable Development, Policy Brief Number 7, 2010).

172 The restrictive terms of patent license over Harvard-DuPont Oncomouse gathered much controversy, probably as a consequence of the fact that DuPont has its core business in chemistry and, hence, was less inclined to respect the traditional social norms of biomedical research: *see* Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research,* 45 HOUSTON LAW REVIEW 1095 (2008).

inventions, but rather an extreme measure[173].

At the end of this analysis on the adverse effects of the commercialization of academic biomedical research, especially with regard to the BDA, combined with some flaws that affect traditional flexibilities provided by the patent regimes, it might be assumed that these are problems confined within the American boundaries, however the dynamics of international relations, national economies and innovation policies deny that assumption.

In spite of debates and unanswered questions about the impact of BDA on academic integrity and efficiency, other developed and developing countries are considering to adopt analogous legislations with the purpose of spurring national innovation[174]. Above all that, a 2003 report of the Organization for Economic Co-operation and Development (OECD) incites universities to look for opportunities to commercialize their inventions by the means of spin-off companies and joint ventures with the biopharmaceutical industry, and explicitly refers to the benefits received

173 Esther van Zimmermann, *Clearinghouse Mechanisms in Genetic Diagnostic, in* GENE PATENTS AND COLLABORATIVE LICENSING MODELS, 63, 63-64, *supra* note 115.

174 With reference to South Africa, Malaysia and the Philippines: *see* Michael S. Mireles, *The Bayh-Dole Act and Incentives for the Commercialization of Government-Funded Invention in Developing Countries,* 76 UMKC LAW REVIEW 525 (2007-2008); with reference to India and the dangerous influence of The Protection and Utilisation of the Public Funded Intellectual Property Bill (PUPFIP) on public science, *see* Hafiz Aziz ur Rehman, *Equitable Licensing and Publicly Funded Research: A Working Model for India?,* 16 SOUTHWESTERN JOURNAL OF INTERNATIONAL LAW 75 (2010). For a critical viewpoint about the exportation of the Bayh-Dole model to developing countries, *see* Bhaven N. Sampat, *Lessons from Bayh-Dole,* 468 NATURE 755 (2010).

by the US institutions[175].

Finally, the provision of public goods such as scientific knowledge and health care has an undoubted supranational, and in some way also international, dimension. National regimes are located in a globalized context, with interlinked domestic policies, reciprocal influences and cross-border externalities. As a consequence, sooner or later, similar problems – and, perhaps, some additional ones for developing countries – are likely to emerge, and models which permit the progress of science as well as the access of scientific benefits need to be explored.

175 OECD, TURNING SCIENCE INTO BUSINESS: PATENTING AND LICENSING AT PUBLIC RESEARCH ORGANIZATIONS (2003).

CHAPTER III

WHEN MEANS CANNOT LEAD TO THE END: PATENT FAILURES IN PHARMACEUTICAL INNOVATION

III.1 A CASE OF DYNAMIC SOCIAL (IN)UTILITY OF PATENT PROTECTION: THE R&D GAP FOR NEGLECTED TROPICAL DISEASES

It was 1997 when the Parliament of South Africa supported Nelson Mandela post apartheid government in its reform of healthcare system. Modeled to address the entrenched disparities between wealthy white niche and black majority as well as the specific concern of the growing HIV/AIDS crisis, it was so approved the Medicines and Related Substances Control Amendment Act. The aim of this legislation was to grant the parallel importation, generic substitution through compulsory licenses and price control of medicines. In February 1998, thirty-nine pharmaceutical companies brought suit against the government of South Africa alleging various violations of the TRIPS Agreement and the South African Constitution176. This lawsuit was actually without merit, however it was not legal argumentations that conducted to its withdrawal.

176 The Pharmaceutical Manufacturers' Association of South Africa et al. v. The President of the Republic of South Africa et al., 4183/98 High Court of South Africa (Transvaal Provincial Division).

Non-governmental organizations (NGOs), with the support of other non-state actors such as universities' researchers, from developing and developed nations, reacted in front of pharmaceutical industry's pressure on South Africa government. They maintained that unconditional TRIPS minimum standards of substantive and procedural protection of patents in the all WTO country Members, regardless of their development levels and national needs, was a disproportionate burden. Thanks to the so-called *Pretoria Case*, civil society has so discovered that a patent rent on pharmaceuticals is one important – if not the most – determinant in the access gap to essential medicines177.

The primary rationale of any patent system is to permit high prices for recouping R&D costs beard by inventors. The traditional internal flexibilities within patent regimes, like research exemptions or compulsory licenses, aim to re-introduce elements of competition in the market of a given patented product so as to allow a decrease of its price. In the pharmaceutical sector, other than an 'access gap', namely the inability for patients, especially for those living in poor countries, to obtain existing medicines because of their high prices, there is a 'research gap'. Thought until now this additional side-effect of patent law in pharmaceuticals has

177 Frederick M. Abbott, *WTO TRIPS Agreement and Its Implications for Access to Medicines in Developing Countries,* Study Paper 2A, UK Commission on Intellectual Property Right (2002).

received less public attention compared to the first one, unfortunately its implications are no less extensive178.

In 2004, the Global Forum for Health Research pinpointed a pressing element of global health disparities and called it the "10/90 Gap" since 'only the ten percent of the world expenditure on health R&D is spent on health conditions that represent ninety percent of the global burden'179.

In particular, the control of diseases like visceral leishmaniasis (i.e. black fever), African trypansomiasis (i.e. sleeping sickness), schistosomiasis, Chagas disease, leprosy, onchocerciasis, guinea worm, hookworm and trachoma180 represents also the key for achieving at least four of the eight Millennium Development Goals (MDGs)181. However it seems very unlikely that these MDGs targets will be achieved by 2015. Furthermore, MDGs and a lot of other initiatives have focused on child mortality, HIV/AIDS, tuberculosis (TB) and malaria leaving a large group

178 Kapczynski et al., *supra* note 158, at 1046-1053.

179 Global Forum for Health Research, *The 10/90 Report on Health Research 2003-2004, supra* note 157.

180 For a list of principal neglected tropical diseases, definition and respective global burden, *see* WORLD HEALTH ORGANIZATION, GLOBAL PLAN TO COMBAT NEGLECTED TROPICAL DISEASES 2008-2015, at 28-34 (Geneva, 2007).

181 In September 2000 it was adopted the UN Millennium Declaration which committed nations to a global partnership to reduce poverty and has been expressed in eight goals to be achieved by 2015. Goals Four, Five, Six and Eight are respectively directed to reduce child mortality, improve maternal health, combat HIV/AIDS, malaria and other diseases, create a global partnership for development. The MDGs Report 2009 warned that overall progress has been too slow for most of the targets to be met by the deadline of 2015. In particular, it remarked the repercussions of the economic crisis also with reference to lower levels of aid from OECD countries in recession seeing that commitments are expressed as a percentage of national income: *see* UNITED NATIONS, MILLENNIUM DEVELOPMENT GOALS REPORT 2009, available at http://www.un.org/millenniumgoals/ (last visited January 26, 2011).

of 'other diseases'182 still neglected. On the contrary, the global failure to invest in new drugs for these diseases has caused severe consequences.

First of all, we must consider that North America, Europe and Japan represented 82.4% of the world pharmaceutical market in 1999, while Africa and Asia, though constituting more than two-thirds of the world population, only accounted for 10.6%183. Of the 1233 drugs developed and commercialized worldwide between 1975 and 1997, only 4 were tailored specifically for neglected tropical diseases (NTDs)184. Many of the existing NTDs drugs were developed more than 50 years ago and often are themselves highly toxic185. Because of NTDs, every year die as many people as were killed by the 2004 tsunami186 though these

182 The reference is to MDG 6 (Combat HIV/AIDS, Malaria and Other Diseases) and its targets: A) halt and begin to reverse, by 2015, the spread of HIV/AIDS; B) achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it; C) halt and begin to reverse, by 2015, the incidence of malaria and other diseases: *see* http://www.un.org/millenniumgoals/aids.shtml (last visited January 26, 2011); David H. Molyneux, *"Neglected" Diseases but Unrecognised Successes: Challenges and Opportunities for Infectious Disease Control,* 364 THE LANCET 380, 382 (2004).

183 Patrice Trouiller, Els Torreele, Piero Olliaro, Nick White, Susan Foster, Dyann Wirth and Bernard Pecoul, *Drugs for Neglected Diseases: A Failure of the Market and a Public Health Failure?,* 6 TROPICAL MEDICINE AND INTERNATIONAL HEALTH 945, 946 (2001) *citing* IMS, *1999 IMS Health Global Insight Report.*

184 Patrice Trouiller and Piero Olliaro, *Drug Development Output from 1975 to 1996: What Proportion for Tropical Diseases?,* 3 INTERNATIONAL JOURNAL OF INFECTIOUS DISEASES 61 (1999).

185 For instance, to treat African trypanosomiasis is used melarsoprol, an arsenic-containing compound developed in the 1940s in order to poison the trypanosomes before affecting the patient: *see* Peter Hotez, Eric Ottesen, Alan Fenwick and David Molyneux, *The Neglected Tropical Diseases: The Ancient Afflictions of Stigma and Poverty and the Prospects for their Control and Elimination,* 582 ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, HOT TOPICS IN INFECTION AND IMMUNITY IN CHILDREN III 27 (2006).

186 According to the World Health Report 2004, some estimates indicate that may result 500,000 annual deaths from the NTDs: *id. at* 23, 25.

diseases cause more global public health repercussions in terms of chronic disability rather than death. So, for example, onchocerciasis prompts blindness and intense itching that turns into chronic skin changes; Chagas disease, chronic and disabling heart conditions. This means that NTDs also have a prominent social impact due to lost educational potential187, reduced economic productivity188 and stigma so much that they not only generate in the context of poverty, but they also promote poverty189.

Currently, worldwide drug development system depend mainly on patent incentive, and so to market forces. This incentive mechanism skews the direction of R&D toward those diseases that assure the highest financial returns while fails where a potential market is not enough "attractive", or else commercially valuable, to replenish R&D costs190. This happens where a market is too small (like the case of orphan drugs

187 Schistosomiasis and hookworm hinder children to learn in school: *see* Charles H. King, Katherine Dickman and Daniel J. Tisch, *Reassessment of the Cost of Chronic Helmintic Infection: A Meta-Analysis of Disability-Related Outcomes in Endemic Schistosomiasis,* 365 THE LANCET 1561 (2005); Peter J. Hotez, Simon Brooker, Jeffrey M. Bethony, Maria Elena Bottazzi, Alex Loukas and Shuhua Xiao, *Hookworm Infection,* 351 NEW ENGLAND JOURNAL OF MEDICINE 799 (2004).

188 Guinea worm and river blindness result in missed days of works: *see* M. P. Little, L. P. Breitling, M. G. Basanez, E. S. Alley and B. A. Boatin, *Association between Microfilarial Load and Excess Mortality in Onchocerciasis: An Epidemiological Study,* 363 THE LANCET 1514 (2004); annually lymphatic filariasis determines the loss of US$1 billion in India alone: *see* K. D. Ramaiah, P. K. Das, E. Michael, H. Guyatt, *The Economic Burden of Lympatic Filariasis in India,* 16 PARASITOL TODAY 251 (2000).

189 Hotez et al., *The Neglected Tropical, supra* note 185, at 26.

190 Jeffrey Sachs, *Helping the World's Poorest,* Center for International Development at Harvard University, available at http://www.cid.harvard.edu/cidinthenews/articles/sf9108.html (last visited January 26, 2011).

for rare illnesses)191 or too poor (such as drugs for tropical neglected diseases)192.

Thus far, whether or not a 'tragedy of the anticommons' in biomedicine has actually occurred remains a vexed empirical question, on the other hand empirical literature demonstrates that strong patents not always spur innovation and the problem of the R&D gap on neglected diseases is a clear evidence. Moreover, in the eventuality that an 'anticommons' should actually exist, it would have even more impact on research for neglected diseases where the financial resources are scarce and coping with increased transaction costs is harder193.

Although governments, private foundations and also pharmaceutical companies194 have already committed funds for neglected diseases

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191 *See* Henry G. Grabowski, *Patent, Innovation and Access to New Pharmaceuticals,* 5 JOURNAL OF INTERNATIONAL ECONOMIC LAW 849, 858, 860 (2002) where it is framed an effective parallelism between the lack of economic incentives which weigh down on neglected diseases and rare illness; Henry G. Grabosky, *Increasing R&D Incentives for Neglected Diseases: Lessons from the Orphan Drug Act,* available at http://econ.duke.edu/Papers/Other/Grabowski/Orphan_Drug.pdf (last visited January 26, 2011) where the same scholar, starting from the previous parallelism, proposes to amend the US Orphan Drug Act of 1983 so as to include market pull mechanisms suitable for neglected diseases. In fact, even if they afflict millions of individuals, from an economic standpoint NTDs are also orphan diseases since as rare illnesses the expected returns are too small.

192 Trouiller et al., *Drugs for Neglected,* supra note 183, at 946.

193 Rai, *Proprietary Rights, supra* note 159; Susan K. Sell, *The Quest for Global Governance in Intellectual Property and Global Heath: Structural, Discursive and Institutional Dimensions,* 77 TEMPLE LAW REVIEW 363 (2004).

194 In 2001, Eli Lilly created the firm InnoCentive to administer a number of commercially sponsored prizes. Later on, some philanthropic organizations such as X-Prize Foundation, the Prize4Life Foundation and the Gotham Prize sponsored prizes for biomedical research: *see* Spring Gombe and James Love, *New Medicines and Vaccines: Access, Incentives to Investment and Freedom to Innovate, in* ACCESS TO

research, the challenge remains costs, in particular their containment. Apart from the current economic downturn, the "diseases of poverty" will always have smaller R&D budgets compared to diseases with high commercial value195.

The existing proposals to face the patent failure of 'research gap' are represented by R&D institutions alternative to patents, designed to boost the market of NTDs and which can be divided into two broad categories, end-to-end (E2E), i.e. proposals in which the reward is given after all innovation steps are completed, and pay-as-you-go (PAYG) solutions, i.e. proposals in which instead the reward transferred at or near the time that each step is executed196. It has also been suggested to design a combination of these push and pull mechanisms into an ad hoc legislation in behalf of pharmaceuticals, an orphan drug-type program on the model of pioneering US Orphan Drugs Act of 1983197 and the subsequent similar laws enacted in Japan and Europe198. Finally, in recent times

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KNOWLEDGE IN THE AGE OF INTELLECTUAL PROPERTY 531, 535 (Gaëlle Krikorian and Amy Kapczynski eds., Zone Books, New York, 2010).

195 Stephen M. Maurer, *The Right Tool(s): Designing Cost-Effective Strategies for Neglected Diseases Research,* Report to WHO Commission on Intellectual Property Rights, Innovation and Public Health 1 (2005) available at http://www.who.int/intellectualproperty/studies/S.Maurer.pdf (last visited April 5, 2010).

196 *Id.* at 28-33.

197 MICHAEL KREMER AND RACHEL GLENNERSTER, STRONG MEDICINE: CREATING INCENTIVES FOR PHARMACEUTICAL RESEARCH ON NEGLECTED DISEASES 68-75 (Princeton University Press, Princeton-Oxford, 2004)

198 For a comparison between the US Orphan Drugs Act and the Regulation (EC) 141/2000 as well as other orphan drugs laws, *see* Hannah E. KETTLER, NARROWING THE

nonprofit actors decided to directly go in for filling the gaps in research funding and production through the establishment of Product Development Private-Public Partnerships (PD-PPPs).199 Typically, these initiatives arise from mixed incentives, including philanthropic contributions by foundations as well as public sector grants and tax credits for the pharmaceutical industry200.

GAP BETWEEN PROVISION AND NEED FOR MEDICINES IN DEVELOPING COUNTRIES (Office of Health Economics, London, 2002).

199 PPPs split in two main categories. One focused on product development (PD-PPPs) and another one concerned with the improvement of access to new drugs by target populations (Access PPPs), *see* Roy Widdus, *Public-Private Partnerships: An Overview,* 99S TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE S1 (2005).

200 Hotez et al., *supra* note , at 28. Thanks to PPPs, pharmaceuticals have also made important contributions, such as Merck through its Mectizan Donation Program or Pfizer through the Zinthromax Donation Program, *see* Gill Walt and Kent Buse, *Partnership and Fragmentation in International Health: Threat or Opportunity?,* 5 TROPICAL MEDICINE AND INTERNATIONAL HEALTH 467, 468 (2000).

III.2 From Alternative Incentives to Invent toward Alternative Sources of Innovation: The Emergence of Public-Private Partnerships

The easiest E2E pull mechanism is obtained by guaranteeing larger budgets and a "boosted demand" from health systems. It is based on the announcement of an immediate and permanent increase in sponsor's expenditures for NTDs drugs. Obviously, this solution works if that boost is long-lasting and large enough. However, the idea that rich countries will indefinite increase their health spending in R&D for poor countries diseases is in general politically unlikely201, and even more now considering that most of OECD countries are experiencing grim economic recessions. Consequently, on one hand, drugmakers might not respond to the funding increase since they fear that it would be later withdrawn. On the other hand, this mechanism tends to be inefficient because sponsors pay the monopolistic prices set by pharmaceuticals202. For this reason, there have been proposed other incentives to drug development at lower cost.

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201 Temporary forms of boosted demand can rarely work to stimulate R&D by pharmaceutical companies because the drug development pipeline usually takes 12-15 years and there are few cases of companies recovering investments within 10 years. Nevertheless, the UK International Finance Facility (IFF) proposed a similar solution to meet the MDGs by the deadline of 2015: *see* Stephen M. Maurer, *Choosing the Right Incentive Strategy for Research and Development in Neglected Diseases,* 84 Bullettin of World Health Organization 377 (2006).

202 Maurer, *The Right Tool(s), supra* note 195, at 16.

The leading E2E model relies on “guaranteed purchase schemes” which, similarly to prizes, assure a predetermined budget but, unlike prizes, where a fixed sum of money is authorized, sponsors promise to buy fixed quantities of drugs at a fixed price if and when R&D succeeds203. One of the most most prominent example of this type of scheme is known as 'AdvancedMarkets'. The Bill and Melinda Gates Foundation together with the Center for Global Development have committed to pay a minimum price for the first two-hundred million treatments of any new vaccine as well as a ninety-five percent contribution for least developed countries vaccine expenditures. Further, they have reserved the right to stop purchases if a substantially better product appears on the market. While it permits to elicit widely scattered ideas, the main limitation of guaranteed purchases, equal to prizes and grants, is that beforehand sponsors must estimate the size of the required reward and overpayments are quite likely204.

In order to promote innovation, public prizes have been promoted by governments since ages. Prizes are distinguished between “targeted” when they specify a particular topic and “blue sky” when they give the freedom to choose solutions and even problems. Prizes are push mechanisms that may act both as E2E and PAYG solutions depending on

203 *Id.* at 17-19.
204 *Id.* at 74-77.

the fact that they are respectively awarded when the product is completed or for intermediate steps. Also grants are issuable ex-ante or ex-post, though they are generally awarded in advance on the basis of recipient's promise to perform. Grants have the problem of overpayments too, however the fear of losing future contributions works to reduce the risk of broken promises by recipients205.

In order to lower the costs of product development, so as to spur drug R&D even when markets are not profitable, other incentives like tax credits and clinical research subsidies have been suggested. More precisely, this sort of push programs, together with a pull mechanism of a seven-year market exclusivity period for any drug with therapeutical properties for rare illnesses, represent the core characteristics of the US Orphan Drugs Act (ODA). Since this Act cover illnesses with a prevalence of less than 200,000 patients in the US and given that over there the prevalence of NTDs is low, this program would be eligible by US pharmaceutical companies in order to invest in R&D for poor countries diseases. Unfortunately, only a small percentage of the approvals for orphan designated indications is targeted to NTDs206 and mainly because there is a lack of market pull incentives, and so profits, in developing

205 *Id.* at 20-23.

206 As of July 2003, only 12 medical compounds were directed to NTDs, representing roughly 5 percent of the orphan drug approvals. *See,* Grabowski, *Increasing R&D, supra* note 191, at 19.

countries.

Even so, nonprofit culture has also its role in health product development. Quite the opposite, private philanthropies and nonprofit companies are gaining the leadership in NTDs projects207. While in the past there were a number of ad hoc collaborations between public agencies and private pharmaceutical companies for the development of drugs with a relevant social impact208, since mid-1990s different ventures in the form of PPPs have emerged in order to combat the "diseases of poverty".

Actually, early PPPs emerged in the mid-1990s simply acquired huge quantities of drugs to achieve price reductions deriving from the combined purchasing power of participating countries and international agencies. Some pilot programs, such as the UNAIDS treatment access initiative that took place in Chile, Ivory Coast, Uganda and Vietnam, were unsuccessful because they left unquestioned the industry's control over prices through patents, consequently did not contribute in appreciable price reductions and a modest number of people took benefits from this program209.

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207 Wellcome Trust-London School of Economics, Pharmaceutical R&D Policy Project, *New Approaches to Funding Drug R&D for Neglected Diseases* 4 (2005).

208 Private philanthropic funding in global health has a long history and a few important actors like the Rockefeller Foundation and the Ford Foundation: *see* http://www.rockefellerfoundation.org/who-we-are/our-history (last visited January 27, 20119 and http://www.fordfoundation.org/about-us/history (last visited January 27, 2011).

209 Udo Schűklenk and Richard Ashcroft, *Affordable Access to Essential Medications in*

The biggest difference between the initial forms of private philanthropy and the recent 'social experiment' of product development public-private-partnerships (PD-PPPs)210 is that the latter has borrowed a 'portfolio management' strategy from the pharmaceutical and venture capital fields. In other words, they promote the development of a range of different candidate products in order to manage the risk of failure in relation with any individual project211. Obviously, the wideness of such portfolios depends on the monetary size and the years of operational experience of each PPP, including cases of sizeable portfolios with more than 25 projects. Mainly with the financial contribution of the BMGF, it is taking place a sort of PPP proliferation212 with new ventures focused on still unmet problems like NTDs.

Thus, PPPs are transforming into “R&D tanks” for NTDs. Now their goal is to directly fill the 'research gap' and, in fact, they have already

Developing Countries: Conflicts between Ethical and Economic Imperatives, 27 JOURNAL OF MEDICINES AND PHILOSOPHY 189 (2002).

210 For an overview of the trends which conducted to the creation of PD-PPs, see Roy Widdus, *Why Public-Private Partnerships for Product Development Emerged and How?* 3, in ROY WIDDUS AND KATHERINE WHITE, COMBATING DISEASES ASSOCIATED WITH POVERTY: FINANCIAL STRATEGIES FOR PRODUCT DEVELOPMENT AND THE POTENTIAL ROLE OF PUBLIC-PRIVATE PARTNERSHIPS (Initiative on Publlc-Private Partnership for Health, Geneva, 2004).

211 These recent initiatives have decided to draw upon skills and typical procedures of the commercial sphere to the extent that it has been coined the term 'free-market' philanthropy: Andre Damon, The Gates Foundation and the Rise of 'Free-market' Philanthropy, available at http://www.worldproutassembly.org/archives/2007/01/the_gates_found.html (last visited January 27, 2011).

212 The most prominent examples of PD-PPPs are the Global Fund for Vaccines and Immunization (GAVI), Roll Back Malaria, the Stop TB Partnership and the Global Fund for AIDS, TB and Malaria.

brought to market new products, such as a drug to treat visceral leishmaniasis developed by the Institute for One World Health (iOWB)213. The Bill and Melinda Gates Foundation (BMGF)214 and other philanthropic organizations have started focusing on the creation of drug development infrastructures in line with pharmaceutical industry management practices215.

All in all, PD-PPPs have similar characteristics and needs. On one side, they have private sector approaches to R&D, but their primary goal is public health rather than commercial goals. On the other, they need the engagement of public agencies, private philanthropies and the industry, but also to work out strategies for ensuring the most efficacious management of interfaces between these contributors. Further, the underlying involvement of the private sector is a source of new research technologies, but it requires a strategy for management of inherent intellectual property rights in order to assure product access in developing

213 Megan Scudellari, *The Profits of Nonprofit,* 25 THE SCIENTIST 54, 55 (2011).

214 The Bill and Melinda Gates Foundation is the biggest private grant-making foundation in the world. It has three main programs: a US program dedicated to improve public education; a global development program to overcome hunger and poverty especially through financial services for the poor; a global health program directed to improve health problems affecting developing countries by means of investments in R&D of new medicines, vaccines and diagnostics: *see* http://www.gatesfoundation.org/programs/Pages/overview.aspx (last visited January 27, 2011).

215 For a general assessment of BMGF mission and earlier outcomes, *see* Robert E. Black, Maharaj K. Bhan, Mickey Chopra, Igor Rudan and Cesar G. Victora, *Accelerating the Health Impact of the Gates Foundation,* 373 THE LANCET 1584 (2009).

countries216.

As a consequence of these further initiatives, the landscape of biomedical innovation appears even more puzzled. At the upstream level, where in the past there was space only for curiosity-driven research, now public-interest entities like universities are increasingly acting as commercial actors. At the downstream level, the leading role for drug development rests with pharmaceuticals, profitable private enterprises by nature. At the same time, new ventures comprising both private and public actors are emerging as nonprofit pharmaceutical organization but with enterprise-alike management strategies217.

Both processes of hybridization have caused broad-spectrum concerns. Other than side-effects deriving from the "corporativization" of universities like increased secrecy and publication restrictions, or patent proliferation and restrictive licensing, the fact that in 2007 the amount spent by BMGF on global health was almost as much as WHO's annual budget218 and that a large part of its expenditures goes to PD-PPPs,

216 Widdus, *Why Public-Private, supra* note 210, at 5-6, 14; Tim Evans, *A Landscape in Rapid Transition, A Role for Public-Private Partnerships in Controlling Neglected Diseases?,* 79 BULLETTIN OF THE WORLD HEALTH ORGANIZATION 774, 774 (2001).

217 Pervez N. Ghauri and P.M. Rao, *Intellectual Property, Pharmaceutical MNEs and the Developing World,* 44 JOURNAL OF WORLD BUSINESS 206, 210 (2009).

218 David McCoy, Gayatri Kembhavi, Jinesh Patel and Akish Luintel, *The Bill and Melinda Gates Foundation's Grant Making Programme for Global Health,* 373 THE LANCET 1645, 1645 (2009).

especially in the form of nonprofit pharmaceutical219, cannot pass unnoticed.

While the issue of NTDs was accompanied by the call for original and modern strategies involving both the public and the private sector so as new and effective medicines would be developed220, there have been raised concerns about the role, effects and lack of accountability of the BMGT as well as other private nonprofit organizations221.

The BMGT plays a crucial role in term of financial contribution to global health needs therefore it is especially welcomed for drugs that hardly pull a profit, on the other hand it has been criticized because of a lack of transparency in its grant-making program222, especially seeing its enormous financial power and policy leverage. In fact, the BMGF funds all the key contributors to global health, from PPPs, NGOs, universities and policy think tanks to supranational organization such as the WHO and the World Bank. Thanks to its funding it is gaining an increasing degree of

219 In 2001 the Institute for OneWorld Health (iOWH) became the first nonprofit pharmaceutical company in the US. Since its creation, iOWH obtained more than US$200 million from the BMGF: *see* Scudellari, *supra* note 213, *at* 54.

220 See Trouiller et al, *Drugs for Neglected, supra* note 183, at 945.

221 Kent Buse and Andrew M. Harmer, *Seven Habits of Highly Effective Global Public-Private Health Partnerships: Practice and Potential,* 64 SOCIAL SCIENCE & MEDICINE 259, 262-269 (2006).

222 Most notably, other than an information gap about its funding, it has been argued that the BMGF, but also other major donors, sets the priorities considering what the foundation defines as important, regardless the demands of developing countries: *see* Devi Sridhar and Rajaie Batniji, *Misfinancing Global Health: A Case for Transparency in Disbursement and Decision Making*, 372 THE LANCET 1185 (2008).

influence over policy agenda of global health223 and some leverage over the voice of civil society. In addition, its grants are mostly awarded in the light of an informal system of personal networks instead of peer-reviewed selection procedures. This aspect is remarkable also because coupled with the issue that, excluding supranational recipients, US-based recipients accounted for 82% of all funding between 1998 and 2007224.

In sum, also the hybridization of nonprofit foundations, so much that they are now called 'venture philanthropies', appears to be a double edged weapon. The combination of features of not-for-profit and for-profit entities for innovation production is a high-potential solution as for global social welfare guidance and management approach, but their success depends on the extent to which a clash of these two cultures is avoided225.

223 For instance, the BMGF has been involved in the health agenda for the G8. Moreover, BMGF, together with WHO, the World Bank, the Global Alliance for Vaccines and Immunization (GAVI), the Global Fund, UNICEF, the United Nations population Fund (UNFPA), and UNAIDS, is part of a self-appointed group of global health leaders known as the H8. *See* McCoy et al., *supra* note 218, at 1650.

224 *Id.*

225 Desmond Johns, *Values and Benefits,* 79 BULLETTIN OF THE WORLD HEALTH ORGANIZATION 773 (2001)

III.3 Democratizing Private-Public Partnerships: Economic Efficiency May Rhyme with Social Justice?

Between public health and biopharmaceutical industry interests, many public actors of industrialized countries have been criticized for acting mostly on behalf of the latter, and for supporting private interests rather than pursuing social benefits, or even acting as a for-profit organization themselves.

The most cited example is the Bayh-Dole Act of 1980 which has allowed U.S. universities (and Stevenson-Wydler Act did the same for national laboratories) to maintain title to patents resulting from federally funded R&D. As a result, in order to file a patent by any university it is not required anymore an explicit waiver from the government agency which funded the research. Since then it is unquestioned that the 'propensity to patent' by universities greatly increased226. This means that academic biomedical research may now serve mixed entwined types of private and public goals. Former non-pecuniary purposes are now turning into pecuniary so as, for instance, an acceptable degree of scientific rivalry has transformed into scientific competition. Not only universities are

226 Robert W. Hahn, *An Overview of the Economics of Intellectual Property* 11, 26-27, *in* Intellectual Property Rights in Frontier Industries: Software and Biotechnology (Robert W. Hahn ed., AEI-Brookings Joint Center for Regulatory Studies, Washington D.C., 2005).

involved in startup biotechnology companies but often their faculties head these firms together with academic research groups227. Moreover, the public interest in knowledge advancement is apparently obtained through individual property rights, namely patent rights. Since scientific knowledge developed by universities is enclosed into patents now, other than public benefits, it offers universities the prospect of commercial gains and, in this way, has remodeled them as commercial actors. While the increase in university patenting probably has in general positively affected the rate of technology transfer to the downstream private research, it seems to imply impediments to subsequent research. In addition, like private pharmaceutical companies, now universities are willing to reallocate efforts to more commercially valuable research, that is on applied work228 but also on more profitable diseases 'rather than toward diseases that cause the most morbidity and mortality'229.

At the same time, the public sector played a crucial role for international intellectual property protection. As already outlined, western governments considered to put forward an international treaty like the TRIPS Agreement in order to pursue their own national innovation policies.

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227 Ghauri and Rao, *supra* note 217, at 206, 210.

228 Wesley M. Cohen, *Does Open Source Have Legs?* 168-169, *in* INTELLECTUAL PROPERTY RIGHTS IN FRONTIER INDUSTRIES: SOFTWARE AND BIOTECHNOLOGY, *supra* note 226.

229 Juan Rovira, *Trade Agreements, Intellectual Property, and the Role of the World Bank in Improving Access to Medicines in Developing Countries,* 4 YALE JOURNAL OF HEALTH POLICY, LAW, AND ETHICS 405 (2004)

They decided to support the private interests of patent owners in order to increase innovation, information disclosure, technology transfer and more generally economic development230. Reasonably, the problem that arose with pharmaceutical patents does not lie as much in having used a typical public law instrument for defining minimum standards of private rights protection, rather than in the absence of a proper balance between short term costs and long term benefits as well as between conflicting interests, in this case represented by the different levels of development of WTO members and their different public health needs231.

Unfortunately, despite the WHO is supposed to have impressive normative powers, its mission is far from be reached. Many times, the agency has been reactive and what happened in relation with the TRIPS Agreement and pharmaceutical patents is the most manifest example. While other forms of global health governance has been proposed, it is really a hard work to reach a global consensus to structure an international legal obligation to secure health needs of poorer populations by wealthy countries232.

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230 Hahn, *supra* note 226, at 20-36.

231 For an overview on the problem of access to essential medicines in relation with the TRIPs Agreement minimum standards, *see* Sangeeta Shashikant, *The Doha Declaration on TRIPS and Public Health: An Impetus for Access to Medicines* 141, 141, *in* ACCESS TO KNOWLEDGE IN THE AGE OF INTELLECTUAL PROPERTY, *supra* note 194.

232 Lawrence O. Gostin, *Meeting Basic Survival Needs of the World's Least Healthy People: Toward a Framework Convention on Global Health,* 96 THE GEORGETOWN LAW JOURNAL 331, 375-378 (2007-2008).

Nonetheless, government agencies have begun to address the need for research on NTDs by participating in PPPs through their national laboratories and universities. Actually academia, in spite of the increasing pressure from patenting and commercialization practices, basically preserves its different cultural self-perception. Cling on its traditional principles of 'open science', it still considers the production and dissemination of knowledge together with the advancement of the human welfare as core purposes. Therefore, the fact that universities manage their patent portfolios as they were for-profit firms implies more a non-compliance with the norms of science and primary university mission, rather than an ineluctable result of academic patenting. If universities would return to consider themselves as key contributions to global public health, their technology transfer offices (TTOs) should adopt additional metrics, other than commercial achievements, for evaluating their performance. As a consequence, current patenting and licensing practices would change in a manner that the ultimate goal of the advancement of the public interest could be satisfied again233.

Besides the envisaged institutional and operative consequences, the Doha Declaration on TRIPS and Public Health has left the priceless legacy of its negotiations in terms of providing the stimulus for policy alternatives

233 Kapczynski et al., *supra* note 158, at 1084-1088.

to Doha-based solutions234. Starting from this point, a number of ideas and proposals has appeared with the aim of encouraging pharmaceutical innovation and perhaps the creation of PD-PPPs is the most promising, and critical, one. It aims to reconcile in an original way the role of private and public sectors in the protection of the two fundamental public goods, knowledge and global health.

While the need of grants and prizes from private philanthropy for the development of new drugs implies the recognition that patents are not the solution, but rather a potential and not complete solution to innovation enhancement, these other mechanisms neither appear to be a panacea, having them advantages and drawbacks too.

However the PD-PPPs are 'social experiments' which have an inborn aptitude to be modeled over the time so as they might become testing ground for a new application of the 'private-collective' model of innovation235.

In some way, PPPs already have a 'do-it-yourself' approach which,

234 Duncan Matthews, *WTO Decision on Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health: A Solution to the Access to Essential Medicines Problem?,* 7 JOURNAL OF INTERNATIONAL ECONOMIC LAW 98 (2004).

235 The 'private-collective' innovation model takes cue from Internet-based innovation community. While in the past the collective or community efforts to provide a public good was explored in the economic literature as 'collective actions', within this new community there are lead-users innovators which free reveal because of the low ability to profit from patenting but also for positive incentives such as product improvement or personal reputation: *see* ERIC VON HIPPEL, DEMOCRATIZING INNOVATION 80-88 (The MIT Press, Cambridge-London, 2005).

among other things, reduces the need to get involved into international patent reforms as a prerequisite for global health improvements236. In fact, they are based on an bottom-up initiatives in which pharmaceutical companies provide their technological knowledge, together with development and distribution expertise, while the public sector and philanthropic donors fund costs and are in charge with the supervision.

Though the UN Millennium Declaration committed rich countries to assign a percentage of their national incomes to meet the MDGs and the CIPR (Commission on Intellectual Property Rights) Final Report called for an increase of public sector funding for R&D on NTDs, public investments and philanthropic donations should not act as a subsidy to their existing pharmaceutical industries. If any similar promotion of the western private sector, or better, of for-profit sector, by government agencies raises disappointment, all the more so there are concerns when philanthropic foundations do it237. In reverse, they have to keep as main focus the 'drug dilemma' for NTDs and they might also act as capacity-builders for developing countries238 so as they may directly contribute to drug R&D

236 *Cf.* Gaëlle Krikorian, *Social Mutations, in* ACCESS TO KNOWLEDGE IN THE AGE OF INTELLECTUAL PROPERTY, *supra* note 194, at 613.

237 McCoy et al., *supra* note 218, at 1651.

238 PPPs are a opportunity for developing countries to build their own capacity to develop drugs, especially for NTDs. Innovative developing countries like Cuba, India and Brazil are advocating the creation of a network for health innovation in developing countries which encourages local innovation, South-South learning, policy research and information sharing. *See,* Carlos M. Morel et al., *Health Innovation*

for combating those diseases that most affect them239.

First of all, given the high degree of public and private interests involved, a boost of information is a necessary starting point. Transparency should not only mean more extended ex-post descriptions of grant recipients, R&D activities and size of expenditures, but also the removal of any bottleneck which impedes any ex-ante contribution to product development. Co-creation means the joint generation of new ideas, information or even products by a firm and its customers. Examples of corporations using this alternative interface include IBM, Nike240 and Nokia, and PPPs should consider it as an important source of ideas and information. Physicians, patients, researchers and the industry should weave a open network of collaborative efforts so as to enhance not only the degree of transparency but also of active and mindful participation from all involved actors.

Networks to Help Developing Countries Address Neglected Diseases, 309 SCIENCE 401 (2005).

239 CIPR (Commission on Intellectual Property Rights*), Integrating Intellectual Property Rights and Development Policy: Final Report,* 33-34 (2002), available at http://www.iprcommission.org (last visited April 5, 2010); Trouiller et al., *Drugs for Neglected, supra* note 183, at 949.

240 James J. Gillespie, *Co-Creation for Pharmaceutical Companies* 1 *(*Center for Healthcare Innovation, 2011) *available at* http://chipress.org/2011/01/07/co-creation-for-pharmaceutical-companies-1-of-10-in-series-on-ten-technology-trends-for-the-life-sciences-industry/ (last visited January 28, 2011) citing NikeiD, a online custom-design application of the famous clothing firm Nike, and a 2003 co-creation project to discover biological markers of Alzheimer's disease to which participate the Food and Drug Administration, the NIH, pharmaceuticals, universities and nonprofit groups.

With the rise of "Virtual Pharmas"241 inside the for-profit sector, it has been suggested that outsourcing may be an appealing model also for nonprofit organizations that, in this way, can concentrate on the management of drug development and rely on networks of contracts, collaborations and licenses for projects' advancement242.

Most "Virtual-Nonprofit-Pharmas" have directed their earlier efforts to quick results with the aim to demonstrate their effectiveness to sponsors and the public opinion, focusing on the modification of known chemical compounds and on off-label testing to adapt existing drugs to treat new diseases243. Later, they have been engaged in the search for high-quality protein drug targets and in pushing their development by agreements with pharmaceutical companies, so much so nowadays they are responsible for most R&D efforts for NTDs. In the long run, the main obstacle for them, from the basic stage of exploratory biology to clinical trial's phase244, is again budget limitations. Going along the drug

241 For the sake of clarity, here the term "Virtual Pharma' is used in its broader meaning including all the structures that collect more resources than they currently have on its own: *see* Love, *supra* note 101. The virtual status of pharmaceuticals has been discussed further so identifying the term 'Extended Enterprise' for those companies which, other than contractual relationships, rely on collaborations and licenses too: *see* Cavalla, *The Extended, supra* note 101.

242 Solomon Nwaka and Robert G. Ridley, *Virtual Drug Discovery and Development for Neglected Diseases through Public-Private Partnerships,* 2 NATURE DRUG DISCOVERY 919-922 (2003).

243 Maurer, *The Right Tool(s),* supra note 195, at 65-66.

244 Quite recently, it has been adduced evidence that all the parts of drug development pipeline can be subject of outsourcing, from the largest to the smallest companies. Even lead-optimization, the stage during which a compound showing some

development pipeline, their next big challenge is determining the best way to translate the results obtained from genomics245 into chemical leads, therefore resources are a terrific constraint. As a result, the enlargement of the number of contributors might be a justifiable solution in terms of underlying cultural, social and economic determinants to global health and right to development, but also terms of economic efficiency and innovation effectiveness246.

Some commentators have tried to consider the open source model as a solution247. The idea of embedding public health policy into open licensing schemes and within user innovation communities might appear unreasonable. Nonetheless, in some ways, it is just the evolution of certain utilitarian perspectives, and their combination with social justice considerations, which underlie patent law. At the same time, with some overlapping elements, it can be seen also as the reflection of the

effectiveness is converted through many steps into a drug candidate, is now entrusted to contract companies. While research stages like target identification or toxicology are outsourced since decades, pharmaceutical companies have been reticent to outsource activities at the lead-optimization stage especially because the data necessary to file patents are generated during this stage: *see* Clark and Newton, *supra* note 101; Cavalla, *A Quiet Revolution, supra* note 101; Crossley, *supra* note 101.

245 Genomics is focused on mapping and analyzing the entire genetic make-up of organisms, that is its genome.

246 For an overview about how the right to health is linked to the right to development and the right to culture, *see* JOHANNA GIBSON, INTELLECTUAL PROPERTY, MEDICINE AND HEALTH: CURRENT DEBATES 61-77 (Ashgate, Farnham, 2009).

247 Stephen M. Maurer, Arti Rai and Andrej Sali, *Finding Cures for Tropical Diseases: Is Open Source an Answer?,* 6 MINNESOTA JOURNAL OF LAW, SCIENCE AND TECHNOLOGY 169-170 (2004-2005).

interchanging role between public and private entities in pursuing reciprocal interests. Though global public health goals do not pertain directly to private actors and are unfamiliar with private ordering mechanisms, indirectly they may be pursued and achieved thanks private-collective contributions. In this sense, PPPs may become an original application of user-innovation community and co-creation concepts in biomedicine.

IV) Open Source Models in Biomedicine: Workable Complementary Flexibilities within the Patent System?

IV.1 From Open Source to Open Science: An Exploration of the Necessary Conditions for Successful Transaction

Looking at the considerable evolution that life science is experiencing, some scholars have even seen "a different kind of scientific revolution" in that, especially in view of a paradigm shift in the values underpinning its development and, thus, a deep breakthrough that solicits the "reconstruction and reevalution" of what it was, for determining what it should be[248].

Whether or not these changes may truly embody a scientific revolution, a number of attempts have been arranged in recent economic and legal literature to overcome the negative effects caused by the privatization of public-interest biomedical inventions and, in particular, to propose mechanisms in order to "clear" patents. Other than "working solutions", such as ignoring or inventing around patents, as well as

248 *See* Hope, Biobazaar, *supra* note 149, at 3-4 (describing Thomas Kuhn's book 'The Structure of Scientific Revolutions" where scientific progress is recognized as an evolutionary process with revolutionary "paradigm shifts").

traditional tools like the use of research exemptions, there have been proposed new collaborative models which would rehabilitate the communal values of science, restore the functions of free access to and use of innovation, and an original way to reconcile both private and public interests in the exercise of IP[249].

One "engine of public availability" adduced to cope with patent proliferation and fragmentation is open source (OS). It is worthwhile to make it clear first that the term *open source* when applied to patents (in this case, to biomedical patents) is necessarily a misnomer being the disclosure of the invention an essential requirement for the grant of the proprietary right. Most importantly there are not source codes outside the software development to be open, where, on the opposite, the OS philosophy is deeply rooted[250].

Open science is a term generally adopted to refer to practices of transparency and sharing in science, like ones adopted in the pre-1980 era. The use of the expression o*pen source* with different attributes (from the broad reference to biology, to the narrower contexts of bioinformatics, genomics, and drug discovery) is useful instead to describe private ordering methods employed to guarantee and maintain the public

249 *See* van Zimmeren, *supra* note 173, at 64.

250 Andrés Guadamuz Gonzáles, *Open Science: Open Source Licenses in Scientific Research,* 7 NORTH CAROLINA JOURNAL OF LAW AND TECHNOLOGY 321, 327-328 (2006).

accessibility of knowledge. Their main strategy is to leverage the distinctive exclusivity of IP rights in order to enable the sharing of intellectual products[251] and to establish a "bazaar"[252], or else commons-based production, in biomedical R&D. In such significance there is a common feature between the idea of contractual-based biomedical research commons and open source software (OSS).

In most cases the recourse to private ordering mechanisms is deployed for intensifying IP protection, that is to expand the monopoly rights granted by IP rights, like the Digital Rights Management (DRM)

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251 In truth, various, sometimes misleading, meanings have been attributed to OS in biomedical field. Sometimes OS is regarded as a set of licensing criteria: *see* HOPE, BIOBAZAAR, *supra* note 149; or a mode of production centered on the concept of 'open and collaborative research': *see* Arti K. Rai, *"Open and Collaborative" Research: A New Model for Biomedicine* 131, *in* INTELLECTUAL PROPERTY RIGHTS IN FRONTIER INDUSTRIES, *supra* note 226; as a metaphor for restructuring networks and flows of information between researchers: *see* Antony S. Taubman, *Several Kinds of Should. The Ethics of Open Source in Life Science Innovation* 219, in *GENE PATENTS AND COLLABORATIVE LICENSING MODELS*, *supra* note 115; and it is also applied making reference to collaborative projects whose license agreements require contributors to share non-patented innovations and potential improvements within organized communities: *see* Open Source Drug Discovery, http://www.osdd.net/ (last visited August 8, 2010). For the sake of convenience, I will refer to Open Source Biology (OSB) for all the projects in biomedical area intended to increase the access to inventions, peers cooperation and data sharing, both where IP rights are contemplated or not. In forthcoming examples, due clarifications to peculiar aspects inherent to each project will be provided.

252 More than the legal instrument of licenses, OS has been well-characterized for its peculiar form of governance, in particular by a contrast between cathedrals and bazaars as icons of organizational structures. *Cathedrals* as top-down, centralized, hierarchical organizations, while *Bazaars* as bottom-up, decentralized, collective organizations: *see* ERIC RAYMOND, THE CATHEDRAL AND THE BAZAAR: MUSING ON LINUX AND OPEN SOURCE BY AN ACCIDENTAL REVOLUTIONARY (O'Reilly 2001). According to this approach, OS in life science would be a manifestation and a translation of the bazaar model, that is, a 'biobazaar': HOPE, BIOBAZAAR, *supra* note 30, at 18, 106-41.

does in copyright[253]. On the contrary, OSS movement got under way with the purpose to counteract copyright expansion in computer programming and, above all, proprietary restrictions on access and use of source codes[254]. During the same period in which "a kind of scientific revolution" arose in biomedicine, comparable changes occurred also into the software area since spin-off companies from universities started to produce proprietary products. The idea of OSS was a way for reacting to the transformation of software in a proprietary commodity. The development of the GPL (General Public License) by Richard Stallman, together with the operating system *Linux* and open clearinghouses like *SourceForge.net,* rapidly demonstrated the effectiveness of OS projects, so much so that OSS has been later employed by governments all around the world as well as private companies, such as IBM[255].

Starting from this achievement in copyright, also "patents communities" have started to take inspiration from OS, and its use of the legal instrument of license, for improving the dissemination of innovation,

253 Severine Dusollier, *Sharing Access to Intellectual Property through Private Ordering,* 82 CHICAGO-KENT LAW REVIEW 1391, 1393-94 (2007).

254 Even if there are nowadays many different OSS licenses, generally they have some essential features: (1) the access to the source code; (2) the right to copy and redistribute, use, modify for personal use, and redistribute modified versions of the software; and, optionally, (3) the automatic application of the license on each new copy as well as derivative or adapted work: *see* STEVEN WEBER, THE SUCCESS OF OPEN SOURCE 5 (Harvard University Press 2004). Put in broader terms, applicable to biomedicine too, (1) credible commitment; (2) competition; and, optionally, (3) copyleft: *see* Janet Hope, *Open Source Genetics: Conceptual Framework* 171, 179-83*, in* GENE PATENTS AND COLLABORATIVE LICENSING MODELS, *supra* note 115.

255 HOPE, BIOBAZAAR, *supra* note 149, at 126-27.

especially for enabling tools and genes whose patentability is currently improbable might be really impeded. Not ignoring the importance of ameliorating patent quality, as well as refining patent scope in biomedicine, the distinctive feature of these initiatives is to use original private strategies, owning the typical strong points of efficiency and adaptability pertaining to commercial private ordering regulation, but endowed with the singularity of incorporating also the public interest to disseminate patented innovation.

Nevertheless, the difficulties for opening patents are wider and more intricate than for copyright. Above all, from the umbrella of open source biology (OSB) come out disparate projects, in which IP has a notable different role, and so different kinds of problems arise[256]. Several projects have not IP rights to guarantee under a license but only contractual right, being the inventions not patented or comprising mere collection of data or discoveries[257], others just display information in the public domain with free access[258]. Pure OSB projects, on the contrary, rely upon contractual

256 Essentially, two main approaches proceed from existing OSB experiments: to design a common where researchers freely share data without any license, or to leverage patents through a peculiar exercise of their exclusive rights in order to not interfere with follow-on developments: *see* Nolan-Stevaux, *supra* note 156, at 292-98.

257 *See, e.g.,* HapMap project, http://hapmap.ncbi.nlm.nih.gov/ (last visited July 16, 2010).

258 *See* Human Genome Project, http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml (last visited July 16, 2010). The power of the Human Genome Project has been to develop standards for data sharing allowing scientific community to access and reuse data in short time: *see* Melanie Dulong de Rosnay and Shirley S. Fung, *Legal and Technical*

means, such as licenses, to change the exercise of property rights within patents and, more precisely, the exclusive rights of patents are exercised in a way to share instead of limit the use of innovation[259]. These experiments are dedicated to properly clear patents through open-licensing mechanisms, with the aim to subvert the IP regime from within, and not to avoid its use, therefore their inherent difficulties range from the nature and some features that patent law bring with itself, to the characteristic limitations of contract law[260].

Accessibility for Life Science Databases, Proceedings of the Second COMMUNIA Conference: Global Science & Economics of Knowledge-Sharing Institutions, Turin, June 2009, where the accessibility of life science databases is assessed by analyzing their access interfaces and their reuse policies.

259 Dusollier, *supra* note 253, at 1394.

260 *See, e.g.,* BiOS CAMBIA, http://www.bios.net/daisy/bios/home.html (last visited July 16, 2010).

IV.2) Open Access Models for Publicly Available Bio-Databases

The rationales behind OSB models are well-explained by the race to sequence the human genome and the subsequent controversies over private ownership of sequencing results.

In the Nineties, the American biologist and entrepreneur Craig Venter, then researcher at the National Institute of Health (NIH), adapted a technique to isolate protein-coding sequences of genes by the use of gene fragments, known as expressed sequence tags (ESTs). ESTs can provide functional information only if matched with other genes with already known functionality, therefore they should not be patentable since not involving an inventive step. However, in 1991 NIH filed patent applications on a number of ESTs which, in truth, claimed not only the gene fragments but also the whole genes and any proteins involved with each expression. Basically, two kinds of defensive motivations explain that choice, such as the concern about Venter's intention to capture those results after his leaving from NIH for establishing an his own private research institute, and, more in general, the ability of private-sector to free-ride on public-sector genomic data. Although these perils were temporarily resolved by the intervention of the pharmaceutical giant Merck that strategically funded gene sequencing and ESTs data mining

through the *Merck's Gene Index Database,* worries for the higher number of proprietary databases threatening the progress of future research remained[261].

In 1999, while the race to decode the human genome was in its apex, and Venter announced his intention to compile a proprietary databank of an another type of sequence information, the single nucleotide polymorphisms (SNP), Tim Hubbard, head of the Sanger Institute in the UK, found an 'irresistible analogy'[262] between the OS movement philosophy and the aims behind the Human Genome Project (HGP), an international collaboration to map and make publicly available the genome sequence. Also with the help of Richard Stallman, *deux ex machina* of the OSS movement and father of the GPL, in the space of a month, Hubbard drafted a license in order to protect genomic data from misappropriation and subsequent locking into proprietary rights. The idea was never implemented because this kind of information was historically released into the public domain, and so, any kind of constraint was considered too restrictive by the genetic research community[263], which preferred to set a number of agreements, the so-called Bermuda

261 *See* HOPE, BIOBAZAAR, *supra* note 149, at 36-38.
262 *Id.,* at 1-27.
263 Kenneth Neil Cukier, *Open Source Biotech: Can a Non-Proprietary Approach to Intellectual Property Work in the Life Sciences?,* available at http://www.cukier.com/writings/opensourcebiotech.html (last visited August 1, 2010).

Principles, in order to secure the free release of pre-publishing data among scientists[264].

An another prominent example of open access database is GenBank, the NIH genetic sequence database which includes an annotated collection of publicly available DNA sequences and is part of the International Nucleotide Sequence Database Collaboration comprising the DNA DataBank of Japan (DDBJ), the European Molecular Biology Laboratory (EMBL) and the GenBank at NCBI (National Center for Biotechnology Information)265. In 2006, NCBI hit the headlines when Ilaria Capua, an Italian veterinary virologist at the IZSVe *(Istituto Zooprofilattico Sperimentale delle Venezie),* freely released a collection of aviarian flu isolates, including multiple H5N1 strains, into its GenBank instead of giving to the WHO database which is restricted to only 15 countries. On the ground of ethical and scientific fairness concerns, Capua adduced that a restricted access to such data would have taken from the most poor, and affected, countries266. Though initially her decision caused an uproar between the scientific community, later it drove to the creation of GISAID (Global Initiative on Sharing Avian Influenza Data), a global consortium

264 Rebecca S. Eisenberg, *Genomics in the Public Domain: Strategy and Policy,* 1 NATURE REVIEWS GENETICS 70, 72-73 (2000).

265 *See* http://www.ncbi.nlm.nih.gov/genbank/ (last visited January 26, 2011).

266 Antonella De Robbio, *Biobanche e Proprietà Intellettuale: Commons o Caveau? 36-37* (Comparazione e Diritto Civile) available at www.comparazionedirittocivile.it (last visited January 26, 2011).

which provides a sharing platform in influenza research267.

267 *See* http://platform.gisaid.org/dante-cms/struktur.jdante?aid=1131 (last visited January 26, 2011).

IV.3) Open Licensing for Publicly Accessible Genetic Databases

From the efforts of the SNP consortium, a group of private companies and nonprofit organizations originated to cope with the alarm of patent applications on SNPs and an inherent potential anticommons[268], it was developed the *HapMap* project whose goal is to identify patterns of common genetic variations, called haplotypes, and employ them as disease markers. *HapMap* embraced a copyleft model based on the GPL license, in the view to permit the access to its haplotype mapping information but, at the same time, to prevent users from filing patents that would block other users access to database information. In particular, *HapMap* pursued an OS approach by using a click-wrap license which required users to register for accessing to the *HapMap Genotype Database* and to agree 'not to reduce others access to the data and to share the data only with others who have made the same agreement'[269]. Afterwards, this policy was abandoned and all data put into the public domain, in part because the primary goal to avoid blocking patents was reached but, actually, also as a result of some problems deriving from the license obligations.

268 For an extended overview on SNP consortium, *see* Robert P. Merges, *A New Dynamism in the Public Domain,* 71 The University of Chicago Law Review 183, 189-190 (2004).

269 International HapMap Project, Data Release Policy, http://hapmap.ncbi.nlm.nih.gov/datareleasepolicy.html (last visited August 1, 2010).

Firstly, it is worth reminding that there were no IP rights to assert. Since haplotype data were not patented, and the *HapMap* database itself does not benefit from US copyright nor *sui generis* database protection, the click-wrap license relied only upon contractual obligations. In order to ensure that third parties were not able to access to data unless agreeing to the same license terms, the license put restrictions on publications based on the data, which could not include such data and, therefore, could not be properly peer-reviewed. Moreover, while *HapMap* license was adopted with the aim to reconcile the public access and the use of haplotype information, as well as the need to permit downstream users to file patents on product developments, the use of complex and ambiguous provisions nullified those ambitions[270].

Is spite of such loopholes and shortcomings affecting *HapMap* policy, its mere existence is able to demonstrate a potential willingness from both public and private sector to translate the OSS model into biomedical research, with the view to re-open science to its traditional sharing norms.

270 Rebecca S. Eisenberg, *Patents and Data-Sharing in Public Science,* 15 INDUSTRIAL AND CORPORATE CHANGE 1013, 1026-28 (2006).

IV.4) Open Licensing Schemes of Patented Biomedical Innovation

This new idea to apply OS principles into biomedical research has represented a breakthrough within the scientific community, and constituted the foundations of other projects. Starting from Hubbard's experiment to shape copyleft licenses for spurring the international transfer of biotechnology among researchers, it has followed a few implementations of this idea directed both to upstream and downstream research.

All the previous examples of attempts to port OS approach from software to biomedical research have bound the reference to this model with regards to the development methodology element, that is the bazaar-style governance, paired to the traditional hierarchical organization, as just another mode of research production or 'project management technique'. However, OS stands out for being an original IP management model as well and, in particular, centered on licensing mechanisms[271].

Ironically, and contrary to the diffused idea that OSS developers are hostile to the concept of IP rights, in OSS movement there are some of the most fervid defenders of copyright. In fact, source developers

271 Guadamuz Gonzáles, *supra* note 250, at 335.

copyright their works in order to maintain control over the future open use of the source code that they developed, and use licensing terms to design the desired OSS model. In other words, licensing terms vary considering how *open* each OSS should be.

In fact, whereas the "bazaar-governance" is recurrent in all OSS models, they can be distinguished into two broad categories, in respect of the use, or not use, of so-called copyleft licenses. Copyleft is a play on the word copyright since OSS communities, relying on this type of license, make an inverted use of copyright to protect their work since the rights of users are set above the ones of owners. According to this concept, developers accord users to copy, modify and distribute the source code, so long as that users agree to keep open their derivative works making use of the same original copyleft license[272].

In patent law the propagation ambition of sharing ideology, aiming to promote the availability of both the original technology and following developments, cannot be obtained through a viral clause like in copyleft, rather with a mechanism of grant-back. This type of arrangement inserted into OSB license terms requires the patent owner to grant the right to use and sublicense any improvements of the patented technology, and essentially gathers users who participate to the project into 'protected' or

272 Natasha T. Horne, *Open Source Software Licensing: Using Copyright to Encourage Free Use,* 17 GEORGIA STATE UNIVERSITY LAW REVIEW 863, 872-79 (2001).

'self-binding' commons pools. The basic common idea of these projects is to translate into biomedical research the use of proprietary rights, i.e. patent rights, to secure access and use of innovation and its derivate works, or better, improvements, for a potential open class of users[273].

IV.4.1) OSB LICENSING FOR NON-PROFIT ORGANIZATIONS: BIOS CAMBIA PROJECT

The Center for Application of Molecular Biology in International Agriculture (CAMBIA) is a non-for-profit research organization located in Australia which was initially focused only on green, that is, agricultural, biotechnology, and it is currently expanding its action toward red, or health, biotechnology as well. The goal of this center is to fill access and research gaps affecting life sciences and, for that purpose, it combines wet-lab development of biotechnological research tools with web-based collaborative development platforms and a patent searching database. It is mainly financed by prominent philanthropic organizations such as the Bill and Melinda Gates Foundation, as well as public national and international funding bodies, but also by subscription fees from CAMBIA members. In 2005, it launched BIOS (Biological Innovation for Open

273 Nolan-Stevaux, *supra* note 156, at 296.

Society) initiative whose fundamental aspect is "Biological Open Source" or "BiOS" licensing. CAMBIA offers two types of BiOS licenses, one for Plant Molecular Enabling Technology (PMET) and one for Health Technologies (even if the latter is still a draft version which requires additional refinement to be used) and each one must be read in conjunction with its own Technology Support and Materials Transfer Agreement[274].

Even though parallels between OSS and BiOS licenses may be quite hazardous, some similarities are detectable. First of all, BiOS licenses permit the "free use", or better a non-exclusive, royalty-free right to use[275], as well as the "free distribution" expressed in the right to sublicense the invention to third parties[276]. Most importantly, they are copyleft-style licenses requiring the licensees to make any improvements available to other members of the BIOS project[277].

It is well-rendered that the basic purpose behind these license terms is to obtain a viral effect in order to re-open science to its traditional sharing norms and enable the access to data. As previously remarked, in patent law such propagation ambition of openness may be performed

274 As of this writing, the latest versions of these licenses are respectively Version 1.5 for PMET and Draft Version 2.0 for Health Technologies, which are available at http://www.bios.net/daisy/bios/mta/agreement-patented.html (last visited August 3, 2010).
275 *Id.* at clause 2.1.
276 *Id.* at clause 2.2.
277 *Id.* at clause 3.1.

through a grant-back mechanism in favor of the patent owner. Exactly, CAMBIA is the patent holder and retains control over technology, firstly licensed and further distributed, so that licensees cannot prevent other licensees from using the patented technology, together with relevant know-how and materials, in the development of different products[278]. In this way, BiOS approach creates a protected commons where the grant-back entails a 'patent "plus" pool' for the benefit of all members of CAMBIA community[279]. As a consequence, CAMBIA deviates from pure bazaar-governance of contributions to research development for a more centralized model where the community members can discuss in confidence the formation and collective defense of their patentable inventions[280].

The creation of these *commons patent pools* is thus beneficial to mitigate blocking-patent and anticommons in upstream biomedical research, but this scheme might be suitable for downstream research as well. By providing a 'one-stop shop', patent "plus" pools would reduce transaction costs and institutionalize the exchange of technical information

278 The OS version of the traditional licensing term grant-back might be 'reverse grant-back' since the control is not directed to an assignment of rights, but rather to prevent blocking patents on the follow-on improvements: s*ee* Sara Boettiger and Dan L. Burk, *Open Source Patenting, 1* JOURNAL OF INTERNATIONAL BIOTECHNOLOGY LAW 221, 228 (2004).

279 Nolan-Stevaux, *supra* note 156, at 304-08.

280 Joseph Eng Jr, *From Software to Life Sciences: The Spreading of the Open Source Production to New Technological Areas,* 24 TEMPLE JOURNAL OF SCIENCE, TECHNOLOGY AND ENVIRONMENTAL LAW 419 (2005).

not covered by patents. Moreover, BiOS-style licenses do not prevent the commercialization of the technology received from the patent holder, whereupon they might be useful for commons pools devoted to drug discovery. When a new drug target would be developed and enclosed inside intellectual information protected by the pool itself, this system might actually decrease the costs necessary to bring that new drug to the market. Since, besides, BiOS-style licenses cover not only patented innovation but also inherent know-how, they favor sharing of any relevant information for drug development too, and may even diminish the costs to meet regulatory standards in the phase of clinical trials[281]. Thus, other non-profit entities, such as public-private partnerships (PPPs) devoted to neglected diseases research, should consider to employ this kind of licenses between partners, in order to discover and develop new therapeutical treatments more quickly and cheaply.

IV.1.2) OSB Licensing for Universities: UAEM and Yale University Project

Another proposal intended to facilitate research on neglected diseases and to improve access and use of biomedical innovation in

281 Nolan-Stevaux, *supra* note 156, at 309.

developing countries is the one put forward by Universities Allied for Essential Medicines (UAEM).

In 2001, then postdoctoral researcher Amy Kapczynski and her collegues at Yale University, together with *Médicines Sans Frontièrs,* convinced the patent owner Yale and the exclusive licensee Bristol-Myers Squibb to permit generic production of *stavudine,* a drug used in antiretroviral combination therapy for HIV/AIDS. Since this memorable decision, this group of students has become UAEM, a worldwide student organization committed to tackle the 'access gap' for essential medicines, but also the 'R&D gap' for neglected diseases affecting poor countries[282]. Combining these two goals, in 2003 UAEM developed a twofold licensing scheme for university patents, taking inspiration from the OS approach to IP management, in order to create 'self-binding commons' supporting the initiatives to address the access and research gaps[283].

In particular, the Equitable Access (EA) license was designed to safeguard the 'freedom to operate' for any licensee that manufacture and distribute the licensed innovation and subsequent follow-on inventions in developing countries. In order to do so, TTOs grant non-exclusive, fair royalty, licenses to commercial entities which provide the patented

282 For past and current UAEM projects, *see* http://essentialmedicine.org/ (last visited August 3, 2010).

283 As of this writing, the latest version of 'Model Provisions for an "Equitable Access and Neglected Disease License" is Version 1.0 available at http://essentialmedicine.org/archive/eal (last visited August 3, 2010).

invention in low-income or middle-income countries. To preserve the availability of an invention and its derivative products, the EA license contains a grant-back provision for any improvement patents, and a cross-license mechanism for any licensee rights that could be used to block production of further innovation. Moreover, EA licenses have an 'automatic open licensing structure' since rights and obligations are extended automatically to any third party notifying, the university and the licensee who developed the end-product, the intention to produce the item in question for sale in developing countries.

In order, instead, to preserve the availability of academic inventions necessary for the research on diseases affecting developing countries, the UAEM drew up a specific Neglected Disease (ND) licensing strategy. In truth, still employing the EA notification structure, this scheme entails more precisely a ND exemption in case universities enter into exclusive licenses for research tools. This license is directed to guarantee the use of licensor technology for carrying out research on neglected diseases anywhere and, also, to market resulting end-products in developing countries. It has been arranged as a very flexible scheme which may be customized on specific needs and surrounding circumstances. Hence, the licensee might be required to grant-back and cross license his improvements, the exemption could be limited to academic institutions

and non-profit entities, or, on the contrary, applied to commercial enterprises, but for a definite list of neglected diseases, or diseases that meet the low-commercial value general standard[284], such as rare diseases[285].

Notwithstanding the evident differences between UAEM and OSS approaches, first of all because the first one does not aspire as much as typical OS philosophy to build an alternative model of knowledge production, parallels are still strong. In particular EA license, as the GPL does in copyright field, leverages the exclusive rights of patents to ensure the freedom to access and operate along the chain of the patented technology development to a potential open class of licensees and, treating all actors symmetrically with a standardized scheme, inserts the key element of competition for permitting a quicker and less expansive production of innovation[286].

284 For an exhaustive analysis of the EA and ND licenses terms, *see* Kapczynski et al., *supra* note 158, at 1031-1114.

285 The first enacted legislation for rare diseases is the U.S. Orphan Drug Act (ODA) of 1983. It assigns the "orphan" status to disorders affecting fewer than 200,000 people in the U.S. or for which there is no reasonable expectation that the cost of R&D investments will recovered in the U.S. market. In 2000, by the means of Regulation EC/141/2000, also the EU adopted a specific legislation on this matter, moreover expanding the definition of orphan's condition to cover also some tropical neglected diseases. Similar legislations exist in Australia and Japan as well.

286 *See* Kapczynski et al., *supra* note 158, at 1090-91.

IV.5) Open Source Platforms for Drug Discovery

As previously said, being the patent system a mechanism designed for spurring innovation based on mere economic incentives, its utilitarian justifications fail with regards to diseases affecting mostly developing countries, whose markets are typically not commercially profitable.

Above all, for many reasons, R&D is particularly costly in the pharmaceutical sector, especially because most drug candidates fail to reach the market after the long and complex clinical trials they are submitted[287]. This aspect, combined with the languishing financial performance and below-average productivity of last years in the pharmaceutical industry, strengthen the lack of incentives to invest resources in low commercial value research[288]. In fact, where drug markets are limited, because too small (like the case of orphan drugs for rare illnesses) or too poor (such as medicines for tropical neglected diseases), patents are not an effective instrument in stimulating innovation and developing new products.

In order to cope with this patent failure directly affecting the

287 Failures can be attributed to the toxicity or carcinogenicity of the compound, manufacturing difficulties, inadequate efficacy, dosage characteristics, and other problems such as economic factors: *see* Emanuel Hassan, Ohid Yaqub & Stephanie Diepeveen, Intellectual Property and Developing Countries: A Review of the Literature 26 (RAND Report 2010).

288 *See* Oxfam International, Investing for Life: Meeting Poor People's Needs for Access to Medicines through Responsible Business Practices (2007).

creation and the enjoyment of two fundamental public goods, such as scientific knowledge and health care, the Tropical Disease Initiative (TDI) established a decentralized and web-based project intended to tackle the problem of low commercial value research for tropical diseases, and has adopted an OS collaboration to identify drug targets and candidates. The idea comes from the acknowledgement by the lawyers Stephen Maurer and Arti Rai, and the computational biologist Andrej Sali, of the convergence between biology and computing. In the same way software developers find bugs and write paches, biologists look for proteins, that is targets, and select chemicals, or else drug candidates. Thus, bearing in mind the so-called Linux Law 'with enough eyeballs all bugs are shallow'[289], they have looked at a bazaar-style governance for the development of tropical diseases cures290.

289 The reference is to Linus Torvalds, who released in the 1994, when he was a computer science graduate at the University of Helsinki, the first official version of the Linux operating system. Any further improvements of Linux has been permitted by the distributed character of OSS collaboration: for an extended overview on the 'ideal type' of OS collaborations, see STEVEN WEBER, THE SUCCESS OF OPEN SOURCE 54-65 (Harvard University Press, Cambridge-London, 2004)

290 A hint to the extension of Linux Law beyond software development field has been made also with regard to open sharing of biobank data since the collaboration between different kind of scientists, from geneticists to statisticians, bioinformatics and epidemiologists, may bring superior research results: *see* Donna M. Gitter, *The challenges of Achieving Open Source Sharing of Biobank Data* (International Conference on Comparative Issues in the Governance of Research Biobanks: Property, Privacy, Intellectual Property, and the Role of Technology, Department of Legal Sciences of the University of Trento, Italy, 2010) *available at* http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1598400. A bright example of the higher benefits deriving from data sharing in science is the case of the stem cell researcher, Shinya Yamanaka. In 2006 he and his team at the Institute for Frontier Medical Sciences at Kyoto University generated Induced Pluripotent Stem Cells

The initiative is divided into two phases. The first one in which volunteers rely on bioinformatics, a biological research method conducted using computers, in order to select drug targets, identify drug candidates that could bind those targets, and estimate the efficacy of each drug candidate. These research efforts are little by little aggregated through the TDI webpage in a similar way Linux incrementally improves its own operating system, and with the purpose to diminish the need for expensive wet-lab experimentation. The second phase involve the participation of *virtual pharmaceutical companies,* or so-called 'Virtual Pharmas', venture capital firms that, after drug candidates selection, outsource development stages to corporate partners and monitor the performance[291].

At the moment the TDI outputs are not protected by IP rights and not linked to any specific OS license. The TDI considers unlikely that pharmaceutical companies manifest an interest in patenting trivial improvements for the low commercial value market of neglected

(iPSCs) from adult mouse fibroblasts and the year later they were able to do the same from adult human fibroblasts. In the aftermaths iPSCs technique for reprogramming adult stem cells to pluripotent stem cells has been notably improved thanks to Yamanaka's choice to share his data within the scientific community: see Antonella De Robbio and Antonella Corradi, *Biobanche in bilico tra proprietà privata e beni comuni: brevetti o open data sharing?,* 1 ITALIAN JOURNAL OF LIBRARY AND INFORMATION SCIENCE 305, 323 (2010).

291 Maurer, Rai and Sali, *supra* note 248.

diseases[292] and, in any case, until the collaboration will be stabilized, the intention is to leave TDI community members the freedom to develop their own licenses[293].

292 Actually TDI deems the use of typical OS viral clauses in drug discovery field not adequate since such scheme would be expensive and legally dubios: s*ee* Leticia Ortì, Rodrigo J. Carbajo, Ursula Pieper, Narayanan Eswar, Stephen M. Maurer, Arti K. Rai, Ginger Taylor, Matthew H. Todd, Antonio Pineda-Lucena, Andrej Sali, Marc A. Marti-Renom, *A Kernel for Open Source Drug Discovery in Tropical Diseases*, 3 PLOS NEGLECTED DISEASES 1, 8-9 (2009) *available at* http://www.plosntds.org/ (last visited August 8, 2010).

293 HOPE, BIOBAZAAR, *supra* note 149, at 311.

CONCLUSION

Recent years have witnessed the changing picture of biomedical innovation. Traditional players, such as universities and pharmaceutical companies, have modified their structure and conduct. In the pharmaceutical industry there have been processes of concentration, through mergers and acquisitions, and, at the same time, of separation of duties. Biotech companies, often comprising spin-offs from universities, license inventions to pharmaceutical firms that act, more and more, as "Virtual Pharmas", outsourcing increasing part of drug development as well as clinical testing to specialist research organizations. In addition, as said, universities have converged their basic research efforts to commercial utilization and exploitation. The number of players in the R&D process has thereby increased and this evolution brings with itself opportunities as well as complications in coordinating and negotiating activities[294].

The performance of biomedical research industry is highly influenced by the policy framework set by governments, in particular with reference to public sector funding and incentives for private investment. In order to promote investments in innovation field, governments, more or less

294 CIPIH Report, *supra* note 137, at 37.

extensively, have finalized a social contract with all potential patentees, granting them a 20-year period of exclusive rights to control the exploitation of their inventions. This market-based incentive for the enhancement of technical knowledge produces allocative distortions in private investments since it implies insufficient incentives when commercial profitability is low, as turned out by the gap in tropical and rare diseases research.

While firms are typical hierarchical structures since centrally coordinated, markets are decentralized and coordinated through price signals. Although network-based production is decentralized as well, the coordination depends on long-term commitments of participants with a direct reciprocity. In this context, it has emerged the distinctive image of OS as a bazaar, wherein contributions are not consciously organized and labor is not divided, but rather distributed, on the basis of voluntary participation and voluntary selection of tasks. Traditional scientific research and OSS are both, by nature, examples of commons-based peer, or else, bazaar, production. In both areas, contributors' primary relationship is not with each other but with the project, and in OSS exactly project's attributes determine also the extension of their ‘freedom to operate’, as reflected in more or less constraining terms of each OSS

license[295].

As said, OSS projects are generally undertaken by a small numbers of individuals who are prospective users of the end-product and are connected by clearinghouse websites for sharing their developments. In a similar way, the TDI has created a web-based community of scientists exchanging research results on tropical diseases, and whose contributions are decentralized and voluntary.

The incentives to enter into OSB projects may be similar to the traditional ones pertaining to OSS programmers that, besides the ego gratification through peer recognition, have a relevant economic connotation as well. In fact, OS constitutes also an alternative business model, and more precisely, a system where financial returns do not derive directly from knowledge exploitation, but rather indirectly from its dissemination. To put more clearly, OSS projects have demonstrated to offer strong signaling incentives for contributors, gained through the publication of their works, who, in doing so, have increased opportunities to obtain job offers, venture capital funding or shares in start-up software companies. Therefore, OSB projects, like for instance the TDI, should be designed to gain enough effectiveness and popularity for permitting the same level of incentives and benefits offered by OSS.

295 *See* HOPE, BIOBAZAAR, *supra* note 149, at 106-11.

However, assumed that these voluntary contributions in OSB projects actually lead to a drug candidate, the following phase of drug development remains in the hands of pharmaceutical manufacturers, and insufficient private rewards persevere as an obstacle for the production of low-commercial value medicines. While in last years philanthropic initiatives have started to get involved in drug discovery activities for tropical diseases, as for example the PATH Malaria Vaccine Initiative, the further stage of drug development remains mainly uncovered. In this context, such non-profit organizations as well as the public sector, might enter into PPPs with private companies owning the necessary capabilities to develop pharmaceuticals, and so act as Virtual Pharmas in charge of monitoring "outsourced" R&D activities.

Given that, notwithstanding ever increasing commitments of wealthiest individuals to philanthropy[296], these programs should have cost containment as a priority, and drug development implies high risks and costs, OS governance may be a useful and workable tool also in this stage of biomedical R&D. In particular, pharmaceutical enterprises involved in the production of low profitability tropical disease drugs should decide for this type of collaboration models but also, more generally, they might opt

296 *See*, for instance, the Giving Pledge initiative whose goal is to motivate American billionaires to publicly pledge their support into charitable causes and explain the reasons behind that choice in a way to induce other individuals to further commitments: http://givingpledge.org/ (last visited August 5, 2010).

for a bazaar-style production in relation with those aspects of drug development pipeline which do not create any significative competitive advantage for the firm. From this derives that OS-style collaborations would represent a notable opportunity also in final stages of the drug development chain such, for example, predictive toxicology testing as well as clinical trial data management[297].

At the same time, private powers involved in IP production traditionally exert a decisive influence in law making and, in recent years, have reached the international arena as well. Powerful big firms gathered in *de facto* "knowledge cartels" have reached to lock in their competitive advantages persuading governments to protect private interests through public ordering. At the same time, this claimed extension of their monopolistic rights has been accepted by governments for securing private investments into cultural and technological production as well as for industrial policy concerns.

Later on, other private actors, such as nongovernmental organizations (NGOs), arrived in the globalized IP regime, and even if not playing in fora dedicated to hard-law negotiations, they have achieved a role as representatives of public interests and for shading light into the

297 *See* HOPE, BIOBAZAAR*, supra* note 149, at 253-54.

adverse effects of expanded exclusive rights on intellectual goods[298].

Nowadays, it appears that the time for the reaction of other private players involved in IP rights system has come. Intellectual commons directly in charge of knowledge production and dissemination originated the OS movement, a process of new 'spontaneous ordering' which has led to the formation of communities of users with group identity[299]. Those commons have also perceived the need to formally regulate the exchange of knowledge goods, constituting both inputs and outputs during the exercise of their skills. In order words, OS licensing serves, at the same time, the private interest of knowledge developers in IP availability and the public interest of cultural and technological progress[300].

The seed of OS is located in copyright field but has extended its roots to patent-based biomedical research. These steps are conveying toward a *privatization* of IP regulation since OS licensing becomes a different way to exert IP management. A model for IP or contract-based agreements in which public interest goals have room, and that now, for this reason, attracts the interest of institutionalized collaborations, such as non-profit organizations and universities, as well as public institutions, like

298 Maskus and Reichman, *supra* note 131, at 18-20; *see generally* SUSAN K. SELL, *supra* note 43, at 121-162.

299 *See* Peter Drahos, *The Regulation of Public Goods, in INTERNATIONAL PUBLIC GOODS AND TRANSFER OF TECHNOLOGY UNDER A GLOBALIZED INTELLECTUAL PROPERTY REGIME, supra* note 131, at 46, 57-59.

300 *See* Dusollier, *supra* note 253, at 1394.

governments and state agencies.

The advocates of OS arguments consider this IP management model as a mean to convey a real change in the law itself. In the framework of software sector, OS philosophy actually entails an unconventional approach to IP law, in which sharing becomes the new norm. On the contrary, OS-style approaches into biomedical research should be considered as just a new way to recoup traditional sharing norms of science and the principle of open access to data. In any case, and exactly for succeeding in sharing goals, often OSS licenses include mechanisms with the aim of contaminating the open scheme applied to the creative work first licensed to derivative ones. By doing so, such licenses present the peculiar feature of producing effects that are not limited, and go beyond, the contracting parties, so that private ordering rules tend to gain a public ordering and a normative dimension[301]. The "public character" of copyleft, that is the viral effect, is obtained by a mechanism which ties together the license and the computer program. Differently, biomedical patented inventions are not commercialized as commodities, but directed to specialized persons, scientists, for specific research purposes. Therefore copyleft element in OSB, if pursued, needs to be designed on totally different premises, but above all faces peculiar challenges.

301 *Id.,* at 1395.

In order to mitigate a potential 'tragedy of anticommons', the answer promoted by the OS movement does not actually reside into the public domain. This neologism coined by Michael Heller mirrors the older concern for a 'tragedy of the commons', caused by an overuse or underuse of intellectual goods. The public domain may still constitute a right choice for securing public availability of inventions which are not source of competitive advantage for their owners, but more likely of costs if patented, like the case of SNP Consortium. However, the decision to leave an invention into the public domain, and so unprotected by the law in case of misappropriation, poses in danger the sustainability of open access and use of innovation. This limitation of public domain clearly explains why OSS projects, in which the lever of copyright is used to maintain the public accessibility of works, are object of evaluation and attempts of translation in biomedical area. In the latter case the strategy shall be to use the exclusive rights of patents through grant-back provisions inserted in license agreements. Other than some competition law concerns deriving from that use of grant-back provisions[302], also the distinction between improvements and a new inventions is crucial, but could be quite intricate, and contractual clauses inserted in existing

302 *See* Boettiger and Burk, *supra* note 278, 229-31 (2004); Robin Feldman, T*he Open Source Biotechnology Movement: Is It Patent Misuse?,* 6 MINNESOTA JOURNAL OF LAW, SCIENCE AND TECHNOLOGY 117, 139-44 (2004).

projects are not always helpful since more often mere statements with ideological flavors[303].

The sharing norm within OS philosophy is truly effective only if it persists along the chain of successive parties. When innovation developed thanks to OSB projects deviates from the protection offered by patents, in whole, like genetic databases, or in part, such as know-how, there is the problem that entire contracts or some contractual clauses are based on pure private ordering mechanisms in a way that *erga omnes* opposability is compromised. Furthermore, seeing that the basic purpose of OSB projects is to widen the dissemination of scientific knowledge and its benefits, and that not only the exercise of IP rights is increasingly global in its effects, but also the enjoyment of those public goods in which IP is involved, some considerations about the impediments deriving from the territorial scope of patents are required, as well as an evaluation of the 'global propensity' of OS licenses for obtaining a worldwide application of licenses' terms[304].

Recently, the success of OSS as a governance structure whose

303 For example, BiOS CAMBIA project is a protected commons based on a licensing mechanism which guarantees a non-exclusive, royalty-free right to access and use of its patents for all the members, on the condition that any improvement, patented or not, is subject to the same contractual obligations, and giving the power to the members to consider as an improvement any other invention that they want to share with the pool. *See* CAMBIA BiOS License for Planting Enabling Technology, *supra* note 89.

304 *See* Dusollier, *supra* note 253, at 1427-33.

methodologies minimize production and transaction costs, and ensure adaptability in case of customization needs, have induced public administrations to cast a glance toward OS as a way to face resource constraints, and obstacles deriving from standardized, but sometimes not interoperable, software programs[305]. On similar grounds, the great anxiety deriving from the privatization of knowledge goods coupled with the discover of OS licensing schemes intended to guarantee knowledge availability by contractual means, led public and public-interest institutions to use private ordering mechanisms as well. For instance, and with reference to the biomedical field, there have been embedded policy goals into contracts with research funding recipients in order to mitigate the adverse effects of patent exclusive rights. An outstanding example is the IP policy of the California Institute for Regenerative Medicine (CIRM), a state agency funding human embryonic stem cell research. While patenting by recipients of public money is allowed, CIRM requires by contract that patented inventions are "readily accessible" to Californian institutions for non-commercial research purposes.

This effort, together with all previous illustrations of university and non-profit organization initiatives for patent regulation, may not only

305 *See, e.g.,* the Open Source Observatory and Repository for European public administrations encouraging collaborative development and improvements' exchange of publicly financed OSS: http://www.osor.eu/ (last visited August 5, 2010).

manifest that a real anti-commons peril exists, but also illustrates that a contractual approach is able to minimize its effects. Although the features of these actions are profoundly different, there are commonalities in rationales for adopting these OS-style funding agreements and licenses. They all reveal that traditional public patent law flexibilities, such as research exemption, are recognized as limited in their effectiveness, not only by individuals engaged in innovation developments, but now also by organizations which fund those activities and where research takes place. These entities have become aware of the potentialities of alternative private ordering mechanisms to guarantee the fulfillment of their inborn public interest goals of scientific progress and access to health care, pursed, in some degree, thanks to public money[306].

The bottom-up approach of OS appears, therefore, not only limited to its peculiar methodology for knowledge development, but also for the propagation of sharing norm and contract-based patent regulation. OS projects typically pursue the propagation ambition through IP rights licensing, however this viral effect of OS licenses has been gradually sought also in other type of agreements pertaining to knowledge production, in order to secure its dissemination. The sharing ethos of OS philosophy which was born with individuals and within private initiatives,

306 *See* Peter Lee, *Contracting to Preserve Open Science: Consideration-Based Regulation in Patent Law,* 58 EMORY LAW REVIEW 889 (2009).

and that it was later extended also to the public sector, now has to make the decisive step toward public ordering.

Private ordering mechanisms have undoubted advantages in terms of efficiency and customization propensity. Nonetheless, their binding effects are by nature limited to the contracting parties, and viral contamination through the lever of IP rights is not always enough to preserve public availability of knowledge, especially when scientific innovation is not protected by patents, as it happens, because of economic or ethical reasons. Therefore, public ordering is still a *lieu* for pursuing the public goals of innovation enhancement and access to the benefits of scientific progress. Public ordering has an inherent viral effect and the insertion of sharing norms in lawmaking, from soft to hard law, might replenish the democratic deficit of IP regime and, at the same time, support a new way to manage IP rights.

A revision of the traditional 'social contract' between governments and patentees is, on the other hand, required. First of all, the utilitarian justifications behind exclusionary tendency of patents are no longer valid when they create obstacles, instead of incentives, to innovation. Moreover OS proved the validity of an alternative model of IP management. The use of patent exclusive rights, as a means to control competitors, and, in turn, to recoup financial investments, is not truly the only option for spurring

innovation. In fact, before in copyright realm of software development, and later in patent-based biomedical research, OS is demonstrating that while proprietary rights may be necessary for avoiding a *tragedy of the commons* in intellectual information, shared proprietary rights are an hopeful answer to a potential *tragedy of the anticommons.*

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