



Issues paper

The importance of incremental innovation for development

Prepared by the Commission on Intellectual Property

Submission to the World Health Organisation's Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH)

Summary

ICC firmly believes that maintaining intellectual property protection for innovation, including so-called “incremental innovation”, assists development, and in particular access to medicines in the developing world. That view was expressed, and its basis explained, by the ICC representatives who met the CIPIH in Brussels on 15 March 2005. This paper confirms that view and explains the reasons for it in more detail. It also addresses some of the specific questions raised by the CIPIH at that meeting.

The paper also seeks to clarify some of the apparent misunderstandings that seem to have arisen in this debate: such as the view (which ICC considers to be misconceived) that it is possible and helpful to distinguish between “incremental” and other forms of innovation; and the failure to appreciate the important distinction between the *existence* and the *exercise* of intellectual property rights. Further, it supports ICC's basic premise through examples of the way in which intellectual property protection has enhanced innovation for the benefit of developing countries.

The patent system encourages innovation and, if the protection conferred by patents is overly prejudiced, there will be a reduction in investment in inventing, developing and commercialising new pharmaceutical and medical technology, to the detriment of everyone, in both developed and developing countries.

1. ICC: Background; Purpose and Scope of Submission

ICC, the world business organization, promotes international trade, investment and open market economies. It firmly believes that the protection of intellectual property stimulates international trade, creates a favourable environment for foreign direct investment, and encourages innovation, transfer of technology, and the development of local industry, all of which are essential for sustainable economic growth.

However, as a result of its broad membership, including not only intellectual property right holders but also third parties affected by others' intellectual property rights, ICC also understands, and has always supported, the need for a proper balance among different interests. In the field of patents, for example, the system should allow those who innovate to obtain and enforce rights protecting their technological innovations, but should also ensure that society as a whole benefits, for example from disclosure of inventions and the dissemination of knowledge. The interests of third parties must also be balanced against rights provided to innovators. In the view of ICC, maintaining this balance is necessary for the continued successful operation, and general acceptance, of intellectual property protection systems.

ICC understands that the issues being addressed by the CIPIH are complex and emotive. ICC is also aware of the ongoing debate in various international and national contexts concerning how the intellectual property systems, and in particular the patent system, are developing and whether the intended balances in these systems meet the requirements of all affected parties.

One particularly controversial area in this debate is the development-related IP concerns which have been raised in several international fora. These concerns tend to focus on patents as related to health issues, but are also raised in other areas, for example copyright.

ICC considers the establishment of the CIPIH to have been an important event in the debate on the role of patents and public health in the developing world. ICC hopes that the CIPIH will advance the debate, and in particular clarify its intellectual property aspects, in respect of which the discussion often tends to become very emotional.

ICC appreciates the opportunity to present its views on IP related aspects of the work of the CIPIH. ICC, with its global and multisectoral membership, has a broad business and industry perspective, not limited to any individual sector. Its membership has a long experience in innovation and patenting in different sectors and countries and wishes to make a constructive contribution to the CIPIH by sharing this experience.

With regard to the mandate of the CIPIH, ICC notes the speech made by Ruth Dreyfuss, Chair of the CIPIH, on November 4, 2004 during the meeting of the CIPIH in India and published on the CIPIH website. Especially, the statement

“Our purpose is ... to consider what incentives and financing mechanisms, and overall policy environment, would be conducive to the investment of more resources (and used more effectively) by industry for R&D on diseases that mainly affect developing countries. ...

Nor is our work just about intellectual property rights. Rather, it is about how the overall policy framework can be made to work better for that purpose.”

It goes without saying that ICC shares the concern expressed by the WHO about the need to improve public health in developing countries. It is in line with views expressed earlier by ICC

that the issue of public health problems in developing countries is very broad, and must be tackled with different means; and that this is not an issue of intellectual property rights alone.¹

Coming then to intellectual property issues, and especially to patent issues, ICC must limit its intervention in view of the multitude of IP/patent aspects which are dealt with under the CIPIH.

ICC has chosen to comment on what in CIPIH terminology is termed “incremental innovation” and related IP/patent aspects. In ICC’s view, this discussion goes to the heart of the functioning of the patent system. That applies not only to developed countries but also to developing countries, and perhaps especially for the development of small and medium-sized businesses and industries in those countries. The issue of “incremental innovation”, as ICC understands the term, is highly relevant as a general issue and is not exclusively linked to the pharmaceutical industry sector.

Under the topic of intellectual property and public health, the CIPIH will be studying “Incrementally Modified Drugs”. While drugs are specifically mentioned as the topic of study, it seems clear from the ongoing discussion and also from the explanation on the CIPIH website under the topic “Innovation and Public Health” - “Non-patent Models of Innovation”, that the term is intended to be given a broad meaning with relevance to the patent system as a whole. It is stated:

“There has always been debate about the patent system, but this has been fuelled in recent years by its extension to new fields of technology including biotechnology, business methods and software – fields where incremental rather than discrete innovation is most common. ...”

The topic of “*incremental innovation*” is also taken up in the “*Third Discussion*” which was opened on the CIPIH website in December 2004.

The basic issue in the ongoing discussions of this topic among the CIPIH members, as ICC understands it, is whether what is termed “incremental innovation” merits patent protection; and that is the issue addressed in this submission.

2. The role of intellectual property

Intellectual property rights encourage creativity and innovation in most fields of technology requiring research. This is certainly true for the chemical and pharmaceutical fields. Research, whether public or private, requires investment. Investment in private research requires some

¹ See ICC paper ‘Further Views on Cross-Border Compulsory Licensing’ Document n° 450/956 Rev. 21 November 2002 page 1- ‘However, it is clear that many factors other than patented drugs play a role in a successful health strategy - including living conditions, medical facilities, nutrition, and means for the distribution and administration of medicine. It is also clear that many pharmaceuticals which are effective in combating diseases in the developing world are not subject to patent rights (see attached table). It has been pointed out that the availability of health services adapted to local needs, efficient distribution systems and tariff and tax free treatment for drugs play an equally important role in ensuring access to medicines¹. In the current negotiations on paragraph 6 of the Doha Declaration on TRIPS and Public Health, it is therefore important to remember that the issue of access to medicines calls for measures and policies that are entirely unrelated to intellectual property, and which will not be resolved by eroding the strength of intellectual property rights.’

expectation of a return on the investment, partly to reward the investment, partly to fuel further research.

Investment in the chemical and pharmaceutical fields is somewhat different from others, particularly the electronics and software fields. The early stage research to identify new drugs, including new chemicals and proteins, is just the start of a long, arduous and uncertain march to the market. These early stage developments, which result in patents, are sometimes 10 or 15 years prior to the commercialization of a product. A large percentage of time, effort and money goes into research to develop a suitable formulation or presentation of the drug, and even more time and money into the running of clinical trials to substantiate the efficacy of the final drug product. The actual costs for clinical trials can run into the hundreds of millions of dollars – with no certainty of success.

The major source of return (whether to the private or public sector funders, or both) is from marketing the small percentage of products that are successful in passing all the necessary tests. If there is no solvent market, there is no expectation of return on investment and therefore no private investment. The only research that can be expected, beyond necessarily limited pro bono work, is publicly-funded research.

Patents, which are particularly important to the current debate, establish a bargain between society and the inventor under which the State grants a finite period of protection in return for a full, publicly-available description of the invention. They have been created by society to ensure that the return during this period, if any, goes to the person who invested in the research. The patent system enables those investing in difficult and risky research and development to recoup their investment and make a return. It also benefits society: providing better products and processes, and advanced knowledge of technological developments which can be freely used once the period of protection expires. In this way, through the operation of the “deal” between society and the inventor, all advances in technology can be sustained. Without this bargain, innovation would be stifled and society would suffer.

As already mentioned, the costs and time necessary to bring a drug to the market are considerable. While the initial patents covering the basic chemical or protein entity are important to encourage the further investment to bring the drug to the market, the length of time afforded protection by such patents - due to the considerable amount of time necessary to develop a suitable formulation and presentation of the drug, and the time to conduct clinical trials - usually does not provide sufficient protection to balance the overall financial investment.

Further, many inventions made during the development of the drug formulation or presentation, while possibly viewed as 'incremental inventions' by some, are actually critical to bringing the drug to the market. Indeed, as a proportion of all patents granted worldwide, very few relate to what may be termed “breakthroughs”. The vast majority cover innovations which build on inventions of others, with the benefit of full disclosure of those inventions in patent specifications. That is what the patent system was designed to encourage. By its very nature, therefore, it encourages inventors to adapt and modify the developments patented by others –

incrementally or in any other way. It would therefore, in ICC's view, be wholly inappropriate not to allow patents for such forms of innovation; and any such change would adversely affect the ability to finance future drug research. The innovation process in the pharmaceutical sector, as for all other scientific sectors, is one of evolution.

3. Patentability criteria – non-discriminatory

The criteria for patentability are clear. Patents are available for any invention, whether product or process, in any field of technology, provided it is new, involves an inventive step and is capable of industrial application. If an invention meets these criteria, it is entitled to patent protection. If it does not, it is not patentable.

Of these criteria, the most relevant here is inventive step. The invention must not have been obvious to a person skilled in the relevant art at the time the application for a patent was first filed, taking into account the state of the art at that time.

There is no common understanding around the world on how this criterion should be applied and TRIPS provides no guidance. The precise manner in which it is applied differs from country to country. It even differs over time within the same country. Significant progress has, however, been made in harmonizing the standard, particularly in the US, Japan and Europe. This harmonized standard should, in ICC's view, in time become the "gold standard" for patents globally. In the meantime, it may be necessary and appropriate, to encourage investment in local research and manufacturing, for developing countries to adopt a lower threshold to provide easy access to patents for local entrepreneurs. But in ICC's view, it cannot be right to require such countries to adopt a *higher* standard of inventive step.

In any event, neither the inventive step requirement, nor the other basic criteria, make any distinction between different types of innovation – for example between "incremental" and "discrete", or between "me too" and "breakthrough" innovations. As with any innovation, all of these have to be judged against the same basic rules, and that, in ICC's view, is entirely appropriate.

To the extent that genuine concerns about patent quality exist, they relate to the whole range of patents. They are not specific to patents for healthcare products, nor to patents for so-called incremental innovations. If such inventions fail to meet the fundamental criteria set out above, patents should not be granted for them; and where patents have wrongly been granted, courts should (and have) corrected those errors – all as part of the international efforts referred to above to ensure that an appropriate balance is achieved between all entities affected by patents. However the fact that there have been some examples of patent-granting authorities applying the criteria incorrectly does not justify fundamental change to those underlying principles.

4. Application of Criteria to Pharmaceuticals

In the context of pharmaceuticals, it has been suggested that patent protection should not be given to inventions comprising different salts, esters or other derivatives of known drugs, different dosage forms or means of administration of existing products, combinations of known products (including fixed dose combinations), nor “mere” new uses of known compounds, (all of which might qualify for the misnomer “incrementally modified drugs”); nor for modifications to medical devices (such as a single-, rather than multiple-dose, syringe).

These suggestions are, in ICC’s view, misconceived. As stated above, if any such inventions do not satisfy the basic patentability criteria, patents should not be granted for them; and if patents are found wrongly to have been granted, courts and patents offices should correct those errors, just as they should for patents in any field and for any category of innovation. This approach should address, and is addressing, concerns about illegitimate extension of patent term, or “evergreening”. There is no need for separate, or new, legislation to deal with this issue. Further, the suggestion that such inventions do not benefit society is wrong. These types of so-called “incremental” innovation generally result in better health outcomes², for example by increasing efficacy, reducing side effects and/or making administration easier, resulting in improved compliance and greater effectiveness.

Additionally, a recent Tufts University report found that the artificial distinction between breakthrough and so called “me too” drugs was not very meaningful, since a review of entrants for new classes of drugs suggests that the reduction of marketing exclusivity for many innovative drugs is due to increased competitiveness in drug development, rather than a “model of post-hoc imitation.”³

5. Existence vs Exercise of Patent Rights

It is important in this debate to understand the distinction between *existence* and *exercise* of patent rights. This distinction is well-established in many other areas. Examples of the ways in which the exercise of patent rights are regulated in ways which are (rightly, in ICC’s view) unrelated to the basic rules for bringing them into existence include: the application of rules of competition law authorities in considering the inherent tension between intellectual property and competition law; determining the price at which certain patented products can be sold (particularly in the healthcare arena); the way in which products requiring marketing approval (such as pharmaceuticals) are categorised and treated by regulatory authorities; and the approach of courts and other tribunals in interpreting the scope of patent claims and determining the remedies to which a patentee is entitled if he establishes that his rights have been infringed.

² “Pharmaceutical innovation is evolutionary and incentive-driven”; Harvey E Bale and Boris Azais; Bulletin of the World Health Organisation, October 2004, 82 (10), .at page 789.

³ “The Economics of Follow-on Drug Research and Development; Trends in Entry Rates and the Timing of Development”; Joseph Dimasi and Cherie Paquette; Pharmacoeconomics 2004; 22 Suppl, 2: 1-14

This distinction is, in the view of ICC, key in the debate on the patentability of incremental innovation, yet seems often to have been ignored or misunderstood. If validly granted patent rights are, in the view of the authorities responsible for policing these issues, being *exercised* in a way that does not benefit society as a whole, and in particular the developing world, then appropriate action can be taken by that authority to regulate that. However it would be inappropriate, and indeed counterproductive, for such “abuses”, if established, to be dealt with by changing the underlying legislation relating to the grant or coming into *existence* of patents themselves.

6. Examples

As has already been said, the vast majority of patents have been granted for inventions which could be categorised as “incremental”. That includes patents in the pharmaceutical and healthcare field, although the point has much broader application.

This is especially true in the case of patent applications by local inventors in developing countries. Such applications would typically be for low technology or “incremental” inventions which form the basis for the development of local businesses and industries.

Examples of the resulting benefits can be illustrated in many ways. We are aware from the discussions between CIPIH members and ICC representatives on 15 March that many examples have already been drawn to the CIPIH’s attention. However, as requested, we include here the examples referred to at that meeting.

We set out below three categories of example of ways in which such innovations have had positive impacts. First, on a geographical basis, explaining how changes in the patent laws of a number of countries have had beneficial effects. We then provide examples of innovations to specific products and processes that could be categorised as incremental, but which have nevertheless brought significant benefit to patients. Not all relate specifically to patients in developing countries, but they do all illustrate and support our basic premise. Importantly, the examples include incremental developments which have been made by entities *other than* the original inventor – demonstrating the point made above about the patent system operating effectively in providing information to the public on an initial “breakthrough” invention enabling others to develop the ideas further, “incrementally” or otherwise, for the public good. These examples fall into two categories: first, examples from outside the pharmaceuticals field; and secondly, examples from the pharmaceuticals and medical devices fields. In ICC’s view, the chances of any of these beneficial developments having been made would have been much lower had the developers not known that patent protection would be available for them. They all, therefore, support the basic ICC view that such protection should be retained for this type of innovation, and that that will benefit development.

6.1 Country basis

6.1.1. Introduction of new patent system: China

The Chinese patent system came into force in 1985. By 2003, over half of the total 105 318 patent applications for inventions, or 56,769, were made by domestic applicants. Most of these would be inventions which could be deemed to be incremental. This represents an enormous previously untapped source of innovation. The benefits to the Chinese economy, and to its people, are plain for all to see.

6.1.2. Introduction of pharmaceutical product patents: Japan and Italy

Both of these countries have changed their patents laws over the last few decades⁴ to allow the grant of patents covering pharmaceutical products, rather than limiting patents in this technology sector to process patents. Both have benefited significantly from the change, through higher investment in pharmaceutical R&D and higher employment in this sector, without the much-feared increase in prices.⁵

6.2. Non-Pharmaceutical Examples

The examples below are inventions in the medical and chemical fields that could be regarded as incremental insofar as they do not constitute breakthroughs but rather improve on previously developed technology.

6.2.1. Detection and removal of scattering in x-ray technology using digital imaging.

X-ray imaging systems for medical applications have been around for quite some time. There remains, however, a number of areas where improvements are necessary. One of these areas is the prevention of the detrimental effects of scattering rays. Many companies, big and smaller, have been working on solving the problem and many inventions have resulted from their research. Examples of patents covering such inventions are US patent 5,825,032 (assigned to Canon), US patent 6,134,297 (assigned to Advanced Optical Technologies) and 6,408,049 (assigned to General Electric). These inventions taken separately can be considered incremental in the sense that none of them seem to represent the ultimate solution to the problem, rather steps towards an ultimate solution. On the other hand, taken together and with other inventions in the same field, they represent a major progress in improving the readability of x-ray images for better and safer diagnostics by physicians.

⁴ Japan in 1976 and Italy in 1978.

⁵ See for example, for Japan: "New Horizons in India, The consequences of pharmaceutical patent protection"; Heinz Redwood, 1994, which refers to there having been an increase in R&D expenditure by pharmaceutical companies in Japan from 6% in 1975 (before the change) to 10.8% of total sales in 1990; and for Italy: "The Impact of Pharmaceutical Patents – The Italian Experience"; G Jori; 1988, which identifies the key benefits from the change in law as being (i) domestic-owned companies becoming stronger, (ii) greater investment in R&D, (iii) no decreasing employment or turnover, (iv) increasing profits, and (v) international groups investing more in Italy.

6.2.2. The metallocene catalysts.

The development of metallocene catalysts to be used for tailoring new polymers is another example of innovation that could be considered incremental.

First metallocene ("Single site catalysts") patents were filed by Professor Kaminsky at University Hamburg in 1981 for making polymers in general. This was followed by patent applications of Exxon in 1983 and Fina Oil in the mid-eighties also for making polymers in general. In the period 1987 -1992 follow-up patents were filed by Hoechst with a specific emphasis on catalysts capable of making polypropylene polymers, cycloolefinopolymers and polyethylene waxes. In 1987 Mitsui filed patents on cycloolefinopolymers made by using metallocene catalysts. All these follow up patents or patent applications (more than a hundred inventions) can be viewed as "incremental". This is a typical example in the chemical industry: one company starts developments built on patents of other companies. The patent system works to encourage innovation.

6.2.3. The plasma technology for coating welding electrodes and other objects

While it is difficult to pinpoint precisely the starting point of the technology, US patent 3,630,770 (assigned to General Electric) is generally considered as a precursor. It deals with binary mixtures of hydrogen and one of argon, nitrogen and helium. French patent 2,251,153 (Aga) describes a ternary mixture of hydrogen, argon and helium in defined proportions. Air Liquide filed patent applications on improvements consisting of the same components in different proportions for various purposes. This is an example where progress results from deeper research on existing mixtures. Again, these improvements can be regarded as incremental but this is how progress develops.

6.3 Product-Specific Examples in the Healthcare Field

The examples below are inventions that could be categorised as being incremental but fulfil the patentability criterion of inventive step. These inventions also provide a substantive benefit for patients:

6.3.1 Wyeth's venlafaxine

Wyeth is a research-based pharmaceutical company that funnels a significant percentage of its revenue each year to research and develop new drugs and new therapies for treating diseases.

In the 1980s, Wyeth researchers developed venlafaxine as an unprecedented antidepressant that works by selectively inhibiting the neuronal reuptake of serotonin and norepinephrine, two naturally occurring neurotransmitters that have been implicated in depression and other mental disorders. Wyeth scientists recognized venlafaxine's promise as an important antidepressant medication and pressed forward with its development. Wyeth launched venlafaxine for the treatment of depression in the United States in early 1994 under the trade name Effexor®. As originally launched, Effexor® was an immediate release dosage form.

Although effective, it was not used in a wide-spread manner, primarily due to the side effects of nausea and vomiting. Patients who could benefit from this unique drug were deprived of an effective therapy due to these side effects.

Wyeth researchers worked to develop an extended-release formulation that could provide adequate blood plasma levels of venlafaxine such that it could be taken once a day. This was a significant advance involving a sufficient inventive step to warrant a patent, since it was unknown if a once-a-day formulation would be therapeutically effective. Not only did Wyeth's research result in a formulation that could be administered once-a-day while maintaining efficacy, thereby making it more convenient for patients and improving compliance, but it also unexpectedly reduced side effects, such as nausea and emesis, as compared to the immediate release formulation. Venlafaxine is now widely prescribed because patients are able to adhere to the dosing regimen and tolerate therapeutic blood levels without lengthy and severe nausea.

The ability of patients to benefit from the power of venlafaxine is to a large extent attributable to the efforts of Wyeth's work on the extended release formulation. Had Wyeth stopped its research efforts after discovering venlafaxine and launching Effexor®, the true potential of this drug would never have been realized.

6.3.2 Baxter's Factor VIII products

Another example of 'incremental' improvement that provides significant benefit to patients is Baxter's continued R&D activities in the Factor VIII area. Factor VIII was originally derived from plasma. While various plasma concentrates containing Factor VIII were available prior to the 1980s, Baxter continued its efforts on numerous improvements, which might be considered 'incremental', to minimize the presence of contaminants or proteins other than Factor VIII in the final product, and thus provide a higher purity Factor VIII product. This is important since Factor VIII products are used to treat haemophilia, and the higher the purity the more effective the treatment. One such incremental improvement was Baxter's development of a purification process using an immunoaffinity step including monoclonal antibodies against Factor VIII. Other purification processes already existed which provided for high purity Factor VIII products, but Baxter's process, which was patented, provided even greater purity.

6.3.3. Zythromax

Erythromycin A was described and patented in the late 1940s. Many incremental modifications have been made to it since then, by a wide range of people. An example is

Azithromycin. This was developed by Pliva, a pharmaceutical company based in Croatia which, at the time, was a developing country. Pliva and Pfizer entered into an agreement relating to the commercialization of the product. This has resulted in drug resistance being overcome (a benefit to patients worldwide), increased income to Pliva and Croatia, and to the product becoming part of Pfizer's donation to the WHO's International Trachoma Initiative to reduce preventable blindness (a direct benefit to people in the developing world).

ICC hopes that the above submissions will be of assistance to the CIPIH in its deliberations and stands willing to discuss its views further with the CIPIH.

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