Medical progress from breakthrough drugs – the source of new therapeutic classes – is widely uncontested, but this is far from true of drugs that embody incremental innovations. With pressures for cost containment over health care spending, their innovative character is barely recognised, and their commercialisation is deterred by public authorities, especially in France.

Such policies run counter to the very logic of technological progress, however. They pay little heed to the therapeutic and economic advantages of incremental pharmaceutical innovation. Paradoxically, they raise risks in the pharmaceutical industry and penalise, rather than promote, the development of future revolutionary drugs.

THE INCREMENTAL LOGIC OF TECHNOLOGICAL INNOVATION

Technological innovation is marked by radical discoveries and advances through which companies have succeeded in enhancing our quality of life. However, this progress is also characterised by the parallel and complementary development of many gradual or incremental innovations. Bit by bit, they provide numerous improvements through a process of trial, error and correction of radical innovations in the course of their large-scale commercialisation and use.

This makes incremental innovation ubiquitous, an integral part of technological progress regardless of the era or sector. This has applied in the high-tech (computers and electronics), automotive, aeronautic, energy and many other sectors since their early days.

For example, the internal combustion engine, in the time since its discovery revolutionised transport, has seen numerous refinements in power, vibration, size, weight, pollution, etc., enhancing the speed, quality and safety of our journeys while consuming less fuel.

Henry Ford revolutionised the automotive market early in the 20th century with his famous Model T (initially sold only in black). In the 20 years following its launch, it went through many changes. It was transformed by many improvements and was equipped with a starter, electric headlights and an enclosed coloured body, providing its users with greater safety.

Computers illustrate this as well. Each new generation of equipment, whether hard drives, processors or software, sees numerous corrections, updates and new versions, brought to market to the benefit of consumers. Notebooks and smartphones are the result of incremental innovations applied respectively to PCs and to mobile phones.

The evolution of digital cameras perhaps shows the incremental nature of technological innovation even more clearly. Their sale really took off early in the 2000s, turning them into an everyday consumer item thanks to incremental innovations applied to earlier models over the years. The first “digital” device launched by Kodak in 1973 weighed 3.6 kg, had a resolution of 0.01 megapixel, and cost US$20,000!

The medical field hardly escapes this rule. Incremental innovation is naturally a factor of progress, whether in medical devices or drugs. It should be noted, however, that incremental pharmaceutical innovation, weighed down by a state-controlled health care system with spending tightly controlled by the public authorities, no longer enjoys recognition, and its ultimate beneficiaries, namely patients, have no voice in this matter.

3. See A. Gelisys and N. Rosenberg, “The dynamics of technological change in medicine,” Health Affairs, 13, No. 3, 1994, pp. 18-46, using the example of the endoscope, with performances that “depend heavily on a continuous flow of refinements” (p. 32). See also Fabio Pammolli et al., Medical devices competitiveness and impact on public health expenditure, a study prepared for the European Commission, University of Florence, July 2005.
Challenging innovation in this form – with the pharmaceutical industry being the sector that traditionally invests most heavily in R&D and that depends intimately on the resulting innovative products – amounts in reality to going up against the very logic of technological innovation and the way it advances.

**INCREMENTAL PHARMACEUTICAL INNOVATION: CRITICISED AND DETERRED**

The pharmaceutical industry is often accused of marketing new products that are really just "copies" of existing drugs (so-called "me-too" drugs) and that supposedly bring no therapeutic progress to patients. However, the fact is that, unlike generics, these drugs are not copies of existing products. While they may be part of the same therapeutic class and treat the same conditions, they have a different molecule, profile, regimen, dosage, speed of action or metabolism. These are "follow-on" drugs in a given therapeutic class, launched after the "pioneer" in the class is brought to market.

"Follow-on" drugs are often under development at the time the pioneer drug is approved. Drug firms work along parallel paths on the same illnesses and may often produce close or similar molecules. According to one study, about two-thirds of follow-on drugs appearing in the late 1990s in the United States were already in the final phase of clinical trials (phase III) before the first drug in their respective therapeutic class was approved.

However, drug policies in various countries seek increasingly to deter this type of innovation, which they wrongly set against "radical" innovation, by having only "pioneer" drugs come to market.

The French case clearly illustrates this trend. Though incremental innovation has the potential to enhance patients’ day-to-day quality of life, through lesser side effects, better acceptability, greater ease of use or observance, etc., it is viewed as not providing any improvement in actual medical benefit. Since 2004, this type of innovation has not even had a place in the evaluation grid of the Transparency Commission, responsible for measuring the therapeutic program of new drugs.

These policies run counter to the logic of the process of innovation and end up delaying the commercialisation of certain drugs at patients’ expense. They also fail to acknowledge the various advantages that incremental pharmaceutical innovation can offer.

**THERAPEUTIC ADVANTAGES**

What makes incremental innovation indispensable is that new drugs, like any new product, are perfectible and often present flaws. When used on a large scale, pioneer drugs often show inadequacies. As noted by two innovation specialists, "[b]ecause the first drug in a new therapeutic class is probably never the optimal version, incremental improvements after initial adoption play an important role in pharmaceutical and biological development."

From a medical standpoint, having several similar drugs provides advantages over the existence of a single drug, even if it is a "pioneer" or revolutionary drug.

First, the fact is that patients react differently to a drug. Sometimes, certain drugs belonging to the same therapeutic class are ineffective or have major side effects on some patients, whereas this may not be the case with other drugs in the same class.

Second, and in connection with the point above, the existence of several drugs with similar therapeutic effects provides...
greater choice to doctors, who are able to prescribe treatments based on each patient’s individual case. The existence of similar active substances – though with a different therapeutic profile – allows for greater personalisation of the treatment prescribed for the same illness.

For example, for beta-blockers used in cardiology, “often, matching a patient to the right beta-blocker is a process of trial and error, as some products simply work for some patients better than others.” Through incremental innovation, the existence of several beta-blockers provides added value for patients and for the doctors treating them.

Finally, incremental pharmaceutical innovation is a source of greater security. In case of withdrawal of a “pioneer” drug or deficiencies in a therapeutic class, doctors are able to replace it with another one providing similar treatment.

According to Wertheimer et al., “In fact, the history of pharmacology is characterised by incremental improvements in the safety, efficacy, selectivity and utility of drugs.” The fact that nearly two-thirds (63%) of products on the World Health Organisation’s essential drugs resulted from incremental innovation illustrates this phenomenon perfectly (see Figure 1).

**ECONOMIC ADVANTAGES**

Incremental pharmaceutical innovation may also present economic benefits that should not be underestimated.

On the one hand, incremental improvements may increase patients’ well-being. For example, by reducing side effects (dizziness, vomiting, digestive problems, pain, etc.) or making a drug more convenient to use (taking it once rather than several times, or orally rather by injection), they enable patients to have more normal lives and to become productive again more quickly. Many patients would doubtlessly be ready to pay more for an improved version of an old drug.

In addition, while pioneer drugs and the firms that sell them benefit from exclusivity, the existence of several drugs in the same class intensifies competition on the pharmaceutical market and broadens choices for patients and third-party payers (insurers as well as governments). Thanks to incremental innovation, pioneer drugs’ period of commercial exclusivity – before follow-on drugs appear – came down sharply, falling from 10.2 years to 1.2 years between 1970 and the end of 1990.14

When drug prices are not reduced artificially by public authorities, contrary to what is generally the case in Europe, these follow-on drugs are usually sold at lower prices to gain market share at the expense of existing products. According to a study dealing with 20 new drugs launched between 1995 and 1999, the year they came to account for more than half the sales of prescription drugs in the United States, all but one of the follow-on drugs were sold at prices up to 70% lower than that of the pioneer drug in their class.15 This competition can thus have the effect of reducing drug expenses. Drugs resulting from incremental innovation may sometimes be sold at a higher unit price than existing products. But overall treatment may turn out to be less expensive and require less additional care (fewer visits to the doctor or the hospital, less nursing care, etc.).

Finally, commercialising incremental innovations offers advantages in terms of business management. These innovations help diversify risks and income sources. This diversification lowers the risks related to the innovating company’s portfolio of activities and ensures the company of a steadier income flow.

Incremental pharmaceutical innovation thereby ensures income continuity for drug firms, because “no mature industry can sustain itself on income from breakthrough innovation

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The advantages of incremental pharmaceutical innovation

As noted by a specialist, companies cannot neglect the role of incremental innovation in the income flows that end up financing its radical innovation. These funds provide for investment both in R&D and in the production and commercialisation of revolutionary new products.17

Any policy that puts artificial limits on the commercialisation of incremental pharmaceutical innovation would thus have the effect of raising drug firms' risks. Paradoxically, this also penalises the development of new pioneer drugs that public authorities claim to encourage.

**CONCLUSION**

Incremental innovations are an integral part of technological progress regardless of the economic sector or industry being considered. Pharmaceutical innovation is no exception in this regard: once new "pioneer" drugs go on the market, they become open to improvement in several areas, whether in terms of side effects, regimen, convenience of use, metabolism, etc. The active molecule may also be modified, enriching the therapeutic class created through this same pioneer drug.

Incremental innovations of this sort provide numerous therapeutic advantages. They offer doctors greater choice in treating their patients. If a drug proves ineffective or presents major side effects, doctors can then prescribe another drug in the same class. The presence of several similar drugs in a class also offers advantages in case one of them is withdrawn.

Incremental innovations also provide economic advantages. Lesser side effects and greater acceptability and convenience of use represent appreciable gains in day-to-day quality of life for patients. The presence of several similar drugs also reduces the commercial exclusivity of the "pioneer" drug in a therapeutic class, providing for more intense competitive pressure on the pharmaceutical market, which happens to be quite heavily regulated.

Incremental innovations also enable companies on the market to diversify their risks and their income sources. Part of the income from incremental innovations also provides for investment in R&D and the development of future pioneer drugs.

Drug policies that are aimed deliberately at penalising these innovations and requiring drug firms to commercialise only "pioneer" drugs end up, paradoxically, having the opposite effect. Rather than favouring therapeutic progress, they hold it back at the expense of patients who expect to see the benefits of new treatments being developed in the future.

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