Evaluation of expenditure on advanced therapy medicinal products

UNIVERSITÀ CATTOLICA del Sacro Cuore
ALTEMS
ALTA SCUOLA DI ECONOMIA E MANAGEMENT DEI SISTEMI SANITARI

In partnership with:

LS CUBE
OUTSIDE THE BOX

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This scientific study was conducted by ALTEMS in collaboration with LS CUBE and with the non-conditioning contribution of #VITA.

The Working Group that over the years has contributed to the drafting and updating of this Study, which is coordinated by LS CUBE Legal firm and was set up in 2020, has included the participation of Prof. **Giorgio Alleva** (Professor of Statistics, Università di Roma La Sapienza), Prof. **Americo Cicchetti** (Professor of Business Organisation, Università Cattolica di Roma and Director of ALTEMS), Prof. **Paolo Gasparini** (Clinician Coordinator, Committee for Advanced Therapies (CAT) of the European Medicine Agency (EMA), Prof. **Mauro Marè** (Professor of Financial Science, Università della Tuscia and Luiss Business School), Prof. **Eugenio Anessi Pessina** (Professor of Business Economics, Università Cattolica del Sacro Cuore) and Ms **Rosanna Sovani** (lawyer and partner of LS CUBE Legal Firm).

#VITA - Value and Innovation of Advanced Therapy Medicinal Products - is a group of pharmaceutical companies specialising in the Advanced Therapy Medicinal Product sector, which aim to promote the dissemination and exploitation of Advanced Therapy Medicinal Products with the following purposes:

- to transparently disseminate knowledge among the various stakeholders of the innovative value and therapeutic benefits of Advanced Therapy Medicinal Products for patients and citizens;
- to ensure that the same stakeholders acquire objective data and facts on the pros and cons of Advanced Therapy Medicinal Products in order to initiate a constructive dialogue to ensure both patients and healthcare facilities prompt access to innovation.

#VITA is formed of: **Bristol-Myers Squibb, Gilead, Janssen, Novartis, Pfizer, PTC Therapeutics, Roche e Vertex.**

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Sommario

Executive Summary

Advanced Therapy Medicinal Products (or 'ATMPs') are biological medicinal products that are classified into four main groups: **gene therapy medicinal products**, **somatic cell-based medicinal products**, **tissue-engineered products** and **combined advanced therapy medicinal products**.

The development of ATMPs brings new opportunities for **the treatment and prevention of a variety of medicinal conditions** (genetic, oncological and chronic diseases) with no alternative treatment options or for re-establishing, correcting or modifying physical impairments in humans, including by correcting genetically-acquired mutations.

From a clinical standpoint, unlike conventional medicinal products, ATMPs consist of genetic material or cells or tissues or combinations thereof, which are:

- often, by their very nature, **absolutely indistinguishable** from the cells and/or tissues of the patient, or
- absolutely **no longer detectable** as in the case of gene therapies for certain organs (retina of the eye, cochlea of the ear, etc.), since it is not medically possible, as well as being ethically incorrect, to subject a patient to retinal or cochlear sampling for follow-up, or
- **detectable only after highly invasive procedures**, e.g. bone marrow harvesting or skin or muscle biopsies, which are potentially life-threatening for the patient as well as being very costly. It would in fact be a case of characterising by gene sequencing or other 'omics' technologies (transcriptomics, proteomics, metabolomics, etc.), individual cells or tissues in order to distinguish the natural cells or tissues of the patient from those treated with ATMPs;

  in addition:

  - they also include **personalised 'algorithms'**, and even more specific and in many cases individualised procedures such as *genome editing* in which the correction of the gene defect is specific to an individual subject and takes place through a completely personal biotechnological procedure through the transfection of people suffering from various diseases;
  - they are goods produced thanks to scientific research in order to

cure disease and that therefore have **long-term effects** on health, people's well-being, productive potential and healthcare costs;
- they are **intangible assets** as their 'physical' substance is only in some limited cases identifiable over time and moreover using costly, invasive procedures that are often harmful to the patient's health;
- they are **products of complex productive processes**, characterised by a substantial research component. In actual fact, they consist of 'live' drugs whose safety and quality is guaranteed by production processes that are very different to those used for 'conventional' medicinal products, which are based on chemical synthesis. For example, ATMPs cannot be sterilised, because this process would destroy the product. It is precisely this innovative nature that makes their production a very complex sector requiring high-quality manufacturing sites able to operate in strict compliance with GMP (Good Manufacturing Practice);
- as a further **feature that distinguishes them from the vast majority of conventional drugs**, after 'transfection' in the body, **the subsequent phase of the production process takes place inside the body and continues over time.** This is the characteristic that allows ATMPs to maintain their curative action and bring about a permanent or in any case very long-lasting improvement in people's health and therefore personal and professional lives. The most recent data already show the persistence of the therapeutic effects of those ATMPs whose clinical trials and therefore patient enrolment started approximately 20 years ago on people's health and therefore personal and professional lives.

From an economic standpoint, ATMPs differ from conventional medicinal products in that they:
- **can be one-shot therapies**, i.e. be administered with a single treatment, unlike the conventional medicinal products and protocols used for other conditions, which entail repeated and regular treatments;
- **produce an obvious temporal misalignment between actual costs**, which are concentrated in the short term, and **future benefits**, which

are spread over a longer time horizon;

- have **high investment costs**, but also **significant clinical, therapeutic, social and economic benefits** for health services and patient health;
- offer new **cure prospects** for patients with medical conditions that, until now, had no therapeutic solution;
- **act directly on the causes of the disease**;
- require a **long and more complex preparation process**, than conventional medicinal products;
- biological medicinal products are produced from patients' own cells, which are harvested in hospital and are subsequently engineered in company manufacturing sites;
- can only be **administered in qualified and specialised centres** and originate from **highly innovative and complex platforms**;
- require, throughout their lifecycle, ongoing maintenance and innovation in order to be updated and to ensure patients the best possible product;
- generate further benefits in terms of **recovered occupational productivity**, for long periods of life, consequently improving its psychological, interpersonal and social aspects, and afford **recovery of economic profitability** (with clear effects on tax revenues) and obvious **direct and indirect savings for the NHS**[1];
- have an impact on other levels of health service care, because they entail the involvement of hospital resources in the care process;
- involve a sharing of responsibility for treatment outcomes between the pharmaceutical industry and the health service, which contributes with know-how and other technologies to support the care process.

If this is the current scenario, there is an urgent need to find solutions for sustainability in the very short term, since **by the end of 2030** it is expected

1 *Page 11-13 of the #VITA Working Group report published in July 2020 "Economic assessment of Advanced Therapy Medicinal Products: characteristics, reasons and proposal for a new economic and accounting approach", which can be downloaded from www.lscube.it*

that approximately **60 new therapies** will have been approved, and could affect a total of approximately **500,000 patients potentially treatable with a gene or cell therapy**.

The volume of resources required to access these therapies and the way they are funded will be decisive factors in the future, because they will determine **the extent to which healthcare systems are willing to bear their costs**. Indeed, due to their great complexity, ATMPs have **high costs** of between 1 and 3 million euros per administration.

The **relevance of these innovative therapies** therefore puts them **at the centre of the discussion on health, future health policy choices and the sustainability of the health service**. This will pose very delicate choice and rationing problems in terms of patient access to the treatments, which **could result in fewer patients being treated than are eligible**.

A **solution** for identifying the resources with which to fund these therapies and innovative payment models must, therefore, be addressed today so as not to arrive unprepared.

This document addresses in great detail **the clinical and economic features of ATMPs that set them aside from conventional medicinal products**, highlighting the **investment characteristics** typical of **capital expenditure** that would require a corresponding **accounting of these therapies as such**. On the other hand, the need to consider the investment component of some public expenditure is obvious and has long emerged in discussions on public accounting and in the harmonised system of national accounts between countries adopted by the UN and the European Union (ESA).

Such as reconstruction would justify – in order to ensure the financial sustainability of the costs and the necessary equity in the choices of administering these therapies to the population – a **new payment method** (**that can be broken down and paid in installments over more than one year and is outcome-based**, i.e. an Annuity Payment Model), a model elaborated in the Study carried out by this Working Group in 2020. This model envisages a **mechanism of risk-sharing between the NHS and producer companies of the potential clinical results**: if the therapy proves to be ineffective at any time during the payment installment period, the NHS will not be required to pay the subsequent annual installments, which will therefore remain at the

manufacturers' expense[2].

This model would allow the NHS to bear the costs of a new therapy over time, as in the case of chronic therapies; therefore, in line with the health benefits obtained and could allow the NHS to allocate healthcare resources in the short-medium term to resolving other 'unmet medical needs'.

However, in order for an Annuity Payment Model to be effectively applied, it is necessary to apply **consistent accounting methods which allow the costs incurred for the purchase of such therapies to be allocated to the financial years in which the payments are expected to be made in accordance with the contractually established due dates**. If, on the other hand, the installments were to be limited to being a mere method of payment with the full cost of therapy being charged to the budget for the year of administration, there would be no significant impact on the NHS.

Italian Legislative Decree no. 118/2011 introduced a particularly significant innovation regarding the review of the concept of financial accrual by introducing the principal of **'enhanced accrual accounting'**. The enhanced financial accrual principle is fully **consistent with an Annuity Payment Model** in that it envisages that the commitment of expenditure for purchases, such as those of ATMPs, takes place when the legal obligation is satisfied, but is charged to the financial years in which it is expected the corresponding payments will be made, in accordance with the contractually established due dates.

It will remain necessary, however, **to introduce a specific provision** whereby the entities referred to in article 19(2), b) point) and letter c) of Italian Legislative Decree 118/2011 spread the expenses incurred for the purchase of ATMPs between the financial years in which it is expected the corresponding payments will be made in accordance with the contractually established due dates and in an amount equal to such payments. The same requirements shall apply to the consolidated financial statements of the Regional Health Service pursuant to article 32 of Italian Legislative Decree 118/2011.

2 *Page 14 of the #VITA Working Group report published in July 2020 "Economic assessment of Advanced Therapy Medicinal Products: characteristics, reasons and proposal for a new economic and accounting approach", which can be downloaded from www.lscube.it*

Applying the accounting criteria suggested in this Study for an effective implementation of the 'Annuity Payment Model' would, in actual fact, result in an **alignment between cash, financial accrual and economic accrual, resulting in the generation of 'good debt' as occurs for investments**. Although, on the one hand, this effect would help healthcare facilities/prescribing centres to effectively apply payment *at result models* and would help the NHS to dilute expenditure for ATMPs over time in line with the expected benefits, on the other hand, the difficulty for the authorities in being able to quantify expenditure for the purchase of ATMPs *ex ante* and control the debt generated *ex post*, could result in them adopting a closed attitude to this proposal, despite the validity of its underlying principles.

In order to overcome this barrier and **allow for a timely programming of expenditure for ATMPs and subsequent monitoring of the expenditure by the relevant authorities**, this Working Group suggests as a solution applying these accounting criteria within the framework of a specific multi-year expenditure authorisation, **by setting up an *ad hoc* fund for ATMPs with the aforesaid accounting characteristics**. Such a Fund could make provision for the allocation of determined sums (thus satisfying expenditure planning and monitoring requirements) and allow for a more appropriate evaluation of the distribution of benefits on a multi-year level within the framework of a controlled management of the expenditure.

1. Good debt, bad debt and healthcare expenditure in the pandemic era

The recent, but in actual fact ancient, distinction between good debt and bad debt is nothing new to economists. For those who deal with macroeconomics and public finance habitually, it sounds apodictic. Public debt is all bad according to certain interpretations, given the effects on saving and the possible displacement of private business. Otherwise, an alternative approach is the Barro approach, whereby debt tends to be neutral and does not lead to major effects on macroeconomic magnitudes or an increase in net wealth. Anticipating that taxes are behind the entity of public debt, taxpayers, who will then be called upon to pay back the interest, do not tend to change their habits – therefore a change in debt does not have significant effects on economic activity. Lastly, according to those inspired by the Keynesian tradition, the effect of debt on income tends to be associated with how the sums are used: therefore, if it is used to finance current consumption or transfers to households and businesses, its multiplier will not be maximised (close to 1) – partly because sooner or later bonuses run out and the budget constraint tends to take effect in the medium-long term; whereas if it is used to finance investment and capital expenditure, it will have a substantial impact on the economic growth of a country – 'good' public debt.

According to the *golden rule*, if debt is used to finance investment, it tends to generate a more or less pronounced increase in income and therefore partly pays for itself and may even help to stabilise the debt:GDP ratio by increasing the denominator. As was stated recently, "*public debt will continue to be sustainable, i.e. it will continue to be subscribed in the future, if used for productive purposes […]. In other words, if it is considered 'good debt' […]. Low interest rates are not in themselves a guarantee of sustainability: the perception of the quality of the debt is just as important*"[3].

Therefore, the really crucial question is not merely the size of the debt (which

3 *Mario Draghi (2020) Rimini Meeting, CL, 18 August.*

nevertheless remains important), its evolution and growth path, especially its ratio to national income, but assessing which uses can make public debt good and sustainable, hence which public expenditure can be financed in deficit. Therefore debt used to finance investment is good, whereas that incurred for current expenditure is less good – even if it can maximise short-term electoral consensus.

This traditional distinction was obviously amplified and brought back to the fore as a result of the spread of Sars-CoV-2, when the European Commission, forced by the catastrophic scenario of the effect of the pandemic on the Member States' economies, opted for suspending European *fiscal rules* – i.e. the budgetary rules that have governed public budgets in the Eurozone since Maastricht – and European state aid legislation, and therefore, ultimately, competition policy in the area. This suspension will however be partial and sooner or later the countries will be called upon to account for their debt and demonstrate its sustainability.

The substantial effect of the pandemic on the economy of the major advanced countries has, however, made it possible to put at the centre of public finance manoeuvres, not only the support of the incomes or the sectors and individuals affected, but also a strong openness to the crucial role played by expenditure on health and healthcare facilities in the different countries, which are fundamental for providing an appropriate and rapid response to the pandemic and its consequences for public health and for stimulating economic recovery.

It then became obvious that health is a key sector for the economic, financial and social sustainability of a country and that every possible effort, preferably coordinated at EU level, is necessary to counteract the epidemic, restore good health to the affected populations and strengthen the reaction capacity of national and local health services.

This situation calls for an innovative approach to improving health services and their effectiveness and efficiency that is unprecedented in the past 50 years. Despite the tragic situation, we are now faced with an extraordinary opportunity to make numerous health innovations, including those based on the modification of the human genome, as widely accessible as possible. This also entails the challenge of adequately accounting for and evaluating

the financial flows associated with the production and distribution of these goods and services in the State budget.
The reallocation of public expenditure and budget priorities, in favour of the human health and health technologies sector – first and foremost to tackle the pandemic, but also to effectively address the treatment of diseases that can be done only now, given the very promising results of medical and biological research – opens up innovative scenarios in terms of both expenditure choices and the economic and accounting evaluation of these new medical therapies. Arguing now that vaccines – as well as advanced therapy medicinal products – are merely a current expense, i.e. the consumption of a good similar to a conventional medicinal product, without medium- and long-term effects, and not an obvious form of investment, no longer seems possible or justifiable.

2. The need for a review of the accounting and capital stock evaluation criteria used by the Eu and the Oecd

It should be pointed out that, beyond depreciation, it is net investment that is crucial for the growth of national income and debt sustainability. Unfortunately, as is common knowledge, over the past decade, Italy and certain other southern Eurozone countries have been characterised by a negative public investment profile, which has been accompanied by a down turn in private investment. This has resulted, in the past ten years, in a sharp decrease in net public capital that has not only reduced stock, but also its quality. Lastly, it is important to consider that "*the obsolescence of the capital goods incorporating new technologies is much faster than that of traditional capital goods*"[4], and therefore it is necessary to prevent a further destruction of net public capital.
Recent technological developments have clearly shown the need to **rethink the concept of capital, both in economic terms and in statistical and nation-**

4 *See Boitani-Giovannini (2021).*

al accounting terms. As a matter of fact, in the traditional accounting approach the notion of capital usually refers to exclusively economic capital, whereas it is clear that human, social and natural capital (associated with the environmental, education and health conditions) is becoming increasingly important for the future of countries.

The approach based on the European tax rules is important and is an essential tool for maintaining the stability of the debts and public finance of the various countries. On its own, however, it could lead to focusing exclusively on liabilities and not also on the endowment of physical, scientific and technological capital, which are crucial for the future of the younger generations and therefore for the economic progress prospects of a country. The global Sars-CoV-2 crisis has made it clear to everyone that environmental protection, climatic conditions and the quality and efficiency of the health service are fundamental assets for the economic and social sustainability of a country.

The opportunity that we have had (and still have) with the resources allocated by the National Recovery and Resilience Plan and the European Commission's Recovery Plan (RRP) and Next Generation EU Plan is therefore decisive and unique for replenishing an adequate net capital stock, particularly in the environmental, healthcare and economic and social sustainability sectors. However, to do so calls for clear innovation at statistical and accounting level: expenditure for traditional and canonical investment must be accompanied by other types of expenditure that current procedures and criteria consider to be essentially current. Remaining on the case of healthcare, could part of the expenditure still considered current, for doctors and healthcare equipment, or in our case, for Advanced Therapy Medicinal Products, ultimately be considered investment, since without them even the 'physical' part of investments in healthcare (e.g. a hospital or therapy administration facility), would not actually be usable[5]?

A **clear example** of the difference that expenditure can have in terms of as-

5 *Expenditure for employee training is accounted for among the costs of a business (therefore an increase in it decreases added value and profits) whereas the purchase of a computer or robot is considered an investment, and is often eligible for tax benefits or subsidies. See Boitani-Giovannini (2021).*

sessing its cash or accrual nature is provided by the very recent case of the **construction super bonus** (110 percent and other schemes). As is common knowledge, the legislation envisaged recognising an amount, to be paid in five and/or ten installments (in the form of a tax credit), equal to the total sum spent. **The accounting of this lesser revenue had been made on a cash basis**, i.e. relating to the actual year in which the tax credit was used and enjoyed in the tax return; and therefore **the effect on public finance and the associated deficit had been estimated and spread over 10 years and in equal parts**.

The decision to accelerate the economic effect of the measure and to **concentrate the use of the credit in the first two years**, in order to stimulate the economy, **changed its nature and valuation for public budget purposes** – it should be remembered that tax expenditure, like tax credits, is in fact identical to equivalent expenditure measures, but implemented on the tax system side. In actual fact, **the potential to bring forward the enjoyment of the credit**, by applying an invoice discount (equal to more or less the overall value of the credit), or even resorting to a complete assignment of the credit through banking channels, have made it completely liquid and have in fact concentrated the sums allocated over time. Anticipating the enjoyment of the credit with respect to the five or ten years considered initially therefore forced Eurostat and the RGS to switch from the cash criterion to the accrual criterion and to earmark, more or less entirely (with an identical effect on public finance balances and therefore on the deficit) the sums allocated for the purposes of the 2021 and 2022 public budgets.

A tax expenditure that should have had an effect over ten year and for which the cash criterion had rightly been used – with only the installment for that year being entered in the annual budget – therefore became a measure with far more concentrated effects on the budget. Making the tax credit fully liquid and payable resulted in its 'loading' for just one or two years, therefore with a concomitant emergence of the cost for the public deficit in those years.

The case of the construction superbonus is highly relevant to the reasoning carried out in this study and shows that **it is possible to consider an expenditure only using the cash (or enhanced cash) criterion**, i.e. according to the time the real financial effects of the expenditure emerge, beyond the time-

line of the payments. **In the first version of the construction super bonus, economic accrual followed the cash criterion, with a pro-rata approach, i.e. the sums only emerged for the current year's installment**. When, on the other hand, the cash was brought forward and concentrated into one or two years, it inevitably had to be accounted for on an accrual basis as well, with the full financial commitment being charged to the public budget, with a consequent impact on the entity of the annual deficit.
Ultimately, the time has come for a radical updating of current accounting criteria, considering that part of current expenditure is required to increase the capital stock and economic assets of a country – therefore its economic sustainability – and that they can therefore be considered, at least in part, as investment expenditure.
As has always been known, accounting criteria are the result of a compromise, which can and must be updated in line with the evolution of technological conditions, the degree of economic development and the common feeling of nations and populations. It is clear that changes to accounting procedures are long overdue; this need, after the Sars-CoV-2 pandemic and the energy crisis causes by the war in Ukraine, is now even more urgent. This situation has made it clear that part of health expenditure has the structural characteristics of investment and systemic effects on income, on wealth stock and on the growth potential of the country.

3. Investment expenditure: an evolving area. Starting points for an economic and accounting assessment

There is broad consensus that investment drives economic growth and business competitiveness. In the definition increasingly adopted in economic literature, investment is expenditure intended to increase the initial endowment of physical, technological, social and human capital.
In the private sector, when evaluating the value of businesses, in addition to the value of the physical and technological capital stock, the value of human and relational capital has long been considered. The methods for calculating the monetary values of these components have also gradually

developed and common calculation standards have been established. Besides, these elements are also taken into consideration when determining the value in bidding for public companies.
However, in the definition of public investment used to delimit the fraction of public capital expenditure that can be considered investment, **reference is still made to the increase in the physical and technological capital at the Administration's disposal, the utility of which is not exhausted in the course of a single financial year**.
Public accounting eludes – perhaps understandably – from a definition of **investment that specifies the purpose of the expenditure from the point of view of the community** and merely lists the different types that comprise it: gross fixed capital formation (the direct investment of pharmaceutical companies); capital expenditure with which pharmaceutical companies fund the investment of other entities (indirect investment); expenditure for the acquisition of financial assets that regard the purchase of participations and shares, capital contributions and the granting of credit for productive purposes.
Each of these types is fully defined in the current manuals for compiling national accounts (SNA and ESA). Starting from the definitions for the components of investment, over time, some public expenditures considered current have been acknowledged as components of investment (software, R&D, military defence systems, etc.)[6]. The history of these steps is important for understanding the reasons behind these new inclusions and the decision-making process that led to these changes.
The need to consider certain public expenditures components of investment is therefore evident, and has long since been brought up in discussions on public accounting standards and the harmonised national accounts systems adopted by the UN (SNA) and by the European Union (ESA). As will be demonstrated below, these are changes that did not call into question the definition of the components of investment, i.e. the distinctive characteristics of the expenditure flows of which it is comprised, rather they regard the classification of the nature of certain categories of expenditure

6 *See UN (2008), Eurostat (2010), Eurostat (2018, 2019). ISTAT (2014), Rgs (2019).*

that were previously classified as current expenditure.
It is starting from the evaluation of the changes most recently introduced into the international accounting systems (1993 and 2008 SNA, subsequently transposed into the 1995 and 2010 ESA) that it is possible to understand how to promote changes that can be shared in terms of content by the entities involved in the decision-making process (i.e. to understand whether it is feasible to account for public expenditure for the purchase of Advanced Therapy Medicinal Products as investment).
As will be described in chapter 5, the innovations introduced with ESA 2010 shed light on significant methodological and operational openings, by admitting, for example, that expenditures for research and development, despite their partial intangibility, represent an increase in the physical and technological capital stock of a country and are therefore, to all intents and purposes, a form of investment. To demonstrate the path undertaken, the Eurostat Committee has set up a number of working groups to evaluate intangible assets and social expenditure (see Appendix A).
Identifying a component of investment for other expenditure items with a mixed nature, such as healthcare and education, appears a more complex matter, as there are evident complexities in their conceptual evaluation, measurement and statistical estimation. In the light of these complexities, the pandemic has made it obvious that the quality of goods and services for health has a strong investment component that can have a considerable impact on the physical, human and technological capital stock of a country and its potential for growth.
Not only that, the central topics economic and social resilience and sustainability in the 2030 Agenda signed by all the countries of the world at the UN headquarters in 2015, constitute the reference framework chosen by the EU Commission for its actions and policy. Resilience and sustainability inspire Next Generation EU policy and the allocation of the corresponding expenditure funds. The review of the Stability and Growth Pact currently in progress could be a golden opportunity to reconsider, at EU level and therefore systemically, the more or less explicit investment component of certain public expenditures.
With regard to evaluating the scope of investments a number of key points can be taken into account:

1. *The definitions and conventions used in national accounting are international*. In principle, it must be possible to compare national accounting data between countries.
2. *The international community regularly updates the definitions and compilation rules for national accounting* in line with changes in the scientific and political-institutional debate, and with the practical feasibility of applying changes to the accounting system.
3. *In the debate and updating process, the alignment between national accounting and the commercial accounting systems is relevant* (*links to commercial accounting*, 2008 SNA, page 433). The International Accounting Standards Board (IASB) has become increasingly important as the entity that sets commercial accounting standards. The IASB issues the International Financial Reporting Standards (IFRS)[7].
4. *The regulation updating process is a lengthy one* (the next SEC update is due by the end of 2025, but it could be expedited due to the pandemic and the openness it has generated regarding investment in healthcare), *and involves working groups, but* ***it can also include intermediate phases with satellite accounts and trials***[8]. They undeniably require a political push from the European Council and/or Parliament and are certainly more likely to be successful if driven by a political push at the national government level.

7 *As is emphasised in the SNA (2008), in most cases, the principles underlying the IFRS are absolutely in keeping with the principles of the SNA. More specifically, it is worth noting that the introduction to the standards explains that economic substance should take precedence over legal form. The pathway for developing new standards that involve over 100 countries in this harmonisation process also appears to be very interesting. In the first phase, a document discussing the arguments for and against a new standard is proposed and published with the initiation of a consultation. Once the comments have been received and analysed, if it is decided to go ahead, an exposure draft is prepared and published for general comment. A formal standard is only developed if this draft receives a substantial favourable comment. In each phase, the available documentation discusses the context of the standard and its formal formulation.*

8 *Satellite accounts can have different characteristics: (a) links to industries or products, sector accounts; (b) links to institutional sectors, a second type of special sector accounts; (c) extension with physical or other non-monetary data; d) links to functions, as in functional satellite accounts; (e) extra details; (f) use of supplementary concepts; (g) changes to certain basic concepts; (h) use of models or inclusion of experimental results.*

4. Current and capital expenditure

As is well known, the **distinction between current and capital expenditure** it not easy and straightforward and it is a question that has been debated by economists for decades. In general terms, it can be said that the distinction remains complex, because it is essentially based on ascertaining the "different duration of the effect produced by goods and services" obtained from the different expenditures. Expenditure is considered to be current if referred to the purchase of goods and services whose "economic utility is exhausted within the accounting year in which the expenditure took place; it is considered to be capital when the effects generated last longer than one year and are spread over several years".
Although trials are ongoing to ascertain the persistence of their effects in the long-term, a considerable number of Advanced Therapy Medicinal Products certainly produce effects that last several years. The fact that public expenditure for the purchase of these therapies constitutes capital expenditure is, in any case, a necessary but not sufficient condition for classifying them as pharmaceutical company investments[9].

5. National accounts reviews: types and recent experiences

In addition to routine reviews typically due to the progressive consolidation of the different sources, from time to time national accountants carry out 'full reviews', also called 'baseline changes' or 'benchmark years', involving far more substantial reviews of the system. The implementation of the new 2008 SNA constituted a substantial general review for all OECD countries. In Europe, the 2010 ESA was enforced by law in September 2014, precisely to take into account the new 2008 SNA.
Besides this exceptional change to the global framework, there are regular 'baseline changes'. The latter consist of four separate operations: 1) the ab-

9 *See the discussion of this point in VITA (2020) www.lscube.it.*

solute values for the year taken as the 'baseline year' are reassessed using statistical sources that are not available every year (population or economic censuses, housing surveys, etc.) with past errors corrected; 2) conventional changes are introduced, in line with the evolution of the international principles for national accounting; 3) the reference year for chain-linked prices is changed; 4) all past data are reassessed using past changes, corrected as necessary for *benchmarking* on the new level of the reference year. This latter operation is known as 'retropolation' or 'back-calculation'.

There are four relatively recent studies on the history of national accounting (Lequiller and Blades, 2014). The preface to the 1993 SNA described the development of the 1953, 1968 and 1993 versions of the SNA. André Vanoli, the French national accounting expert, provides an overview in 'A History of National Accounts' (Vanoli, 2005). Angus Maddison, in the introduction to 'The World Economy: Historical Statistics' (OECD, 2003), describes the very first attempts at measuring national income. 'Double Entry' (Gleeson-White, 2011) provides a very entertaining history of national accounting that links it to the early developments of corporate accounting in the golden age of the Venetian merchants.

As far as the accounting of investment is concerned, what new developments were introduced with the reviews of the last two SNAs?

In the **1993 SNA**, the scope of investments was broadened to include expenditure for software, mineral exploration, artistic originals and valuables. More specifically:

- **expenditure for software** (practically insignificant before the 1970s) was treated as a current cost. In the 1993 SNA, all expenditure for software is instead treated as capital formation;
- mining companies have tended to treat **exploration expenses** (for finding new deposits) as capital expenditure, and the same approach was adopted in the 1993 SNA. Note that exploration costs, regardless of whether something is found, are nevertheless treated as capital expenditure;
- **artistic originals** refer to the production of original films, audio recordings, manuscripts, etc. These expenditures result in future earnings, for example, in the form of royalties;

- **valuables**, such as paintings, antique objects, jewellery and precious metals that are purchased as 'stores of value'. Under the previous systems, the majority of these expenditures for valuables would have been included under expenditure for household consumption.

In the **2008 SNA,** the scope of investment was broadened to include **expenditure for research and development (R&D) and for military defence systems**. More specifically:

A after decades of discussion, it was decided to include **expenditure for research and development** under **gross fixed capital formation rather than current expenditure**, despite the difficulties associated with this change. One of the difficulties is that in most countries, corporate accounting principles treat R&D as current expenditure. As a result, it is difficult to obtain robust and satisfactory data. On the other hand, many countries have a long history of collecting research and development statistics, according to the Frascati manual, which has proven to be an important source of information;

B **expenditure for large-scale military defence systems** is capitalised. The new SNA also considers large military weapons – warships, ballistic missiles and tanks, etc. – fixed capital (it is interesting to note that single-use products, like ammunition, missiles, rockets and hand grenades are considered military inventories).

As evidence of ongoing discussion and review work concerning possible updates to national accounting systems, the Eurostat Committee promotes a number of informal working groups. Eurostat has commissioned consulting firms to produce a number of *issue papers*. In 2018, a informal working group promoted by Eurostat was set up to specifically analyse expenditure on intangible assets (Issue paper for discussion drafted by *PricewaterhouseCoopers* on *Accounting treatment of intangible assets with a view to financial reporting requirements under the future European Public Sector Accounting Standards*, EPSAS). Other working groups are tasked with discussing environmental expenditure and the accounting treatment of social benefits (EPSAS Issue paper drafted by *Ernst & Young on Accounting treatment of intangible assets*).

To conclude, the SNA and the ESA are continuously updated statistical systems that are increasingly widespread and evolve in step with new developments in the economy. One interesting feature is that the measurement of the GDP has been systematically changed under the different versions of the SNA into a broader concept, thus progressively extending the production frontier and increasing the GDP. This happened again with the 2008 SNA, with the capitalisation of research and development and military defence systems. This process is likely to continue. For example, the concept of human capital, which is not within the scope of the 2008 SNA, will become increasingly relevant to the economies of EU and OECD countries in the future. Its incorporation into national accounting would once again expand the frontiers of production.

6. Advanced Therapy Medicinal Products as investment expenditure

A crucial question for Advance Therapy Medicinal Products is whether they can be considered investment expenditure, capable of producing long-term effects. It could be argued that some medical protocols and some advanced therapies (from vaccines through to Advance Therapy Medicinal Products) have evident elements of investment. Advanced Therapy Medicinal Products appear to possess very specific economic and industrial characteristics: the cost of R&D, the systemic effect on patients' life expectancy and QALYs[10]; the effects they have on the individual productivity of patients and on the general productivity of the economic system[11] are evident. On the

10 *Challenges for Economic Evaluations of Advanced Therapy Medicinal Products: A Systematic Review Antonio Olry de Labry-Lima, PhD, Angela Ponce-Polo, MSc, Leticia García-Mochón, PhD, Marta Ortega-Ortega, PhD, Daniel Pérez-Troncoso, PhD, David Epstein, PhD.*

11 *It should be pointed out that, under the 2010 SEC, expenditure for R&D into Gene Therapies is considered investment expenditure, instead of intermediate costs, as was the case in the 1995 SEC, as it contributes to the accumulation of productive capacity through intangible fixed capital.*

basis of the above considerations, could we therefore consider expenditure for Advanced Therapy Medicinal Products fixed investment, with effects on accounting and public finance rules[12]?
This chapter provides input for assessment in order to answer this question, firstly on an economic level, in terms of the impact of such expenditure on capital stock and human development and subsequently on the national accounting standards level.

The characteristics of Advanced Therapeutic Medicinal Products (ATMPs)

Advanced Therapeutic Medicinal Products, as defined by Regulation (EC) no. 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) no. 726/2004, can be classified in three main groups: **gene therapies (which also include genome editing), somatic cell therapies, tissue-engineered therapies or combinations thereof and with other specific devices (e.g. pumps, injectors, etc.) developed an/or adapted for the specific purpose**[13].
Within the broader category of ATMPs, **Gene Therapies** aim to treat a disease directly from its genetic basis, by providing the body with a correct copy of the defective gene or another gene able to compensate for its malfunctioning in the cells affected by the disease and can be *in vivo* or *ex vivo*, in order to cure very serious diseases. **Compared to conventional medicinal products, these therapies are far more complex to research, develop,**

12 *Article 56 of Italian Legislative Decree 118/2011 provides that for expenditure commitments: "1. All legally perfected obligations payable, from which expenditure is incurred for the Regional Authority, shall be entered in the accounting records when the obligation is perfected, and charged to the financial year in which the obligation falls due. Expenditure shall be entered in the accounting records, even if it does not result in actual cash movements.". However, the problem remains as to how investment expenditure is to be properly accounted for and recognised in the budget. The legislation would appear to confirm that investment expenditure is not to be recorded in the financial year in which the financial coverage is identified, rather it should follow the state of progress rule.*

13 *https://www.ema.europa.eu/en/human-regulatory/overview/advanced-therapy-medicinal-products-overview*

produce and then distribute and make available to the general public and health services[14]. They are characterised by a high cost profile, reflecting the costs of production (particularly R&D costs), delivery and management and the commercial sustainability of these therapies.

Advanced Therapy Medicinal Products are highly innovative therapies and can be either **'curative' or 'transformative'**[15], i.e. able to change the natural history of the disease of a patient. Very briefly, the following aspects should be noted:

A these therapies have a particular health and economic profile and specific technical peculiarities. Their essential health characteristic is that they are potentially ***one-shot*, patient- or niche-specific**; i.e. they are **administered in a single treatment**, unlike the conventional medicinal products and protocols used for other diseases, which entail repeated and regular treatments;

B they have high investment costs, but also **significant clinical, therapeutic, social and economic benefits for health services and patient health**;

C they **offer new cure prospects for patients with medical conditions that**, until now, **had no therapeutic solution**;

D unlike therapies aimed at mitigating the symptoms of a condition, advanced therapy medicinal products **act directly on the causes of the disease**;

E given their specific characteristics, they **require a long and more complex preparation process, than conventional medicinal products**;

F they consist in biological medicinal products composed of cells, tissues, genes and/or gene modifications or combinations thereof that produce a therapeutic, prophylactic or diagnostic effect. More specifically, gene therapies consist in introducing 'recombinant' DNA into the patient's body or in directly modifying the patient's genome. **These medicinal products are therefore largely composed of the patients' own cells, which are harvested in hospital then subsequently modified and engi-**

14 *See Jorgensen-Kefalas (2017).*

15 *See Chapman et al. (2019).*

neered in company manufacturing sites;

G they **can only be administered in qualified and specialised centres** and originate from highly innovative and complex platforms;

H they **require, throughout their lifecycle, ongoing maintenance and innovation** in order to be updated and to ensure patients the best possible product.

As far as the more technical aspects of advanced therapy medicinal products are concerned, on the industrial and organisational level it is necessary to consider that:

- they constitute a shift in the main paradigms on which aspects such as the trial, development, production and approval of conventional medicinal products have been based for years;
- they change discovery, product engineering, innovative trial design for the preclinical and clinical phase (i.e. they are in fact designed to suit the specific characteristics of a single individual, something that has already forced national and international regulatory authorities to completely review their evaluation of the experimental designs for the approval of these therapies); the same applies to the manufacturing systems – with regard to their management and scale up – and the final testing on the product to be placed on the market;
- they aim to cure rare or ultra-rare diseases and therefore require special effectiveness/benefit assessment methods for marketing authorisation that are largely different from those approved to date;
- the access procedures are different, as is the selection of centres that can administer these therapies;
- considerable adjustment is required for their pricing and funding.

Worldwide, there are approximately 16 thousand products at different stages of development in the pharmaceutical pipeline, of which one thousand are at phase two or three of clinical trial. To date, in Europe, 23 Advanced Therapy Medicinal Products have been approved – of which 7 were subsequently taken off the market (more than 30%) – most of them for single-gene diseases, blood cancers and tissue lesions. In this case, failure is not due to

scientific aspects, such as safety or effectiveness, but to obstacles regarding the sustainability of these innovative but complex therapies. As a result, in Europe, but also in Italy, despite the positive outcome of their regulatory review and clinical trial, these therapies are not available for our patients[16].
If this is the current scenario, there is an urgent need to find solutions for sustainability in the very short term, since by the end of 2030 it is expected that approximately **60 new therapies will have been approved**[17], and could affect a total of approximately **500,000 patients potentially treatable with a gene or cell therapy**[18].
It is a revolution for patients and for society. On the subject of costs, in the second half of the 1990s, a cancer therapy cost approximately 4 thousand euros, in 2010 it cost 45 thousand euros, in the period 2015-2020, with immunotherapy, it cost 70-100 thousand euros, whereas advanced therapy medicinal products have costs of between approximately 300 thousand and approximately 2.5 million euros. The high cost of these therapies (especially gene therapies) poses a clear challenge for public budgets and public health services[19].

Current financing of Advanced Therapy Medicinal Products

Today's ATMP market is characterised by an historical track record that has, to date, permitted Regional Authorities and/or Local Health Authorities to purchase these therapies thanks to two qualifying factors:

- classification as innovative medicinal products;
- access to the single fund for the regional reimbursement of expenditure

16 *https://www.raggix.eu/snr/quintarelli-bambino-gesu-dal-2009-in-europa-ok-a-23-terapie-avanzate/*

17 *https://www.sciencedirect.com/science/article/pii/S2329050121000668#bib2*

18 *Estimating the Clinical Pipeline of Cell and Gene Therapies and Their Potential Economic Impact on the US Healthcare System - Casey Quinn, PhD, Colin Young, PhD, Jonathan Thomas, BSc, Mark Trusheim, MSc the MIT NEWDIGS FoCUS Writing Group, Center for Biomedical Innovation, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA.*

19 *Page 7 of the #VITA Working Group report published in July 2020 "Economic assessment of Advanced Therapy Medicinal Products: characteristics, reasons and proposal for a new economic and accounting approach".*

for innovative medicinal products pursuant to the 2022 Italian Budget law.

ATMPs are currently financed through the Innovative Medicines Fund unified by the 2022 Italian Budget Law, which also provided for an increase in the Fund's funding of 100 million euros for 2022, 200 million euros for 2023 and 300 million euros for 2024.
Despite the unification of the Fund, the current ATMP financing model continues to have a series of critical characteristics that delay (where they do not hinder) their adequate distribution, which is incompatible with the current estimates analysed in the chapter above: in 2030, it is anticipated that as many as 60 new gene and cell therapies will be launched worldwide, with the potential to concern a total of 500,000 patients with an average cost per therapy of between 1 and 2 million euros.
Indeed, the problem of classifying ATMPs (personalised therapies for single patients) as medicinal products, while it has so far partially simplified the issue of access to reimbursement, has inevitably compressed (if not distorted) the nature of these 'therapies' into a category (that of innovative medicinal products) with a fund that is subject to **very restrictive rules**:

- the 36-month maximum duration of the drug's innovativeness limits access to the fund;
- the fund is split between the various regions on a *per capita* basis rather than based on the regions that are home to the centres where the therapies are administered, thus generating passive mobility problems;
- access to the fund is on an out-of-pocket basis and it can only be invoiced by the (few) Regional Authorities with affiliated centres by means of mobility compensation through direct billing, thus generating passive mobility problems;
- Regional Authorities only accrue the right to reimbursement for the expenses incurred for their residents on an out-of-pocket basis and are forced to advance the sums, with a cascading impact on Local Health Authorities and on prescribing centres.

Rules that are not compatible with the intrinsic characteristics of ATMPs in both clinical and economic terms as we will see below.

The economic characteristics of Advanced Therapeutic Medicinal Products (ATMPs)

When it comes to their economic analysis, Advanced Therapy Medicinal Products have very particular characteristics: they **have a high temporal asymmetry between the emergence of the costs** – which are almost all *up-front* – **and that of the benefits**, with a clear misalignment between costs and benefits. The former are essentially concentrated into a specific year – or the first few years – in which the financial need for expenditure emerges; whereas the latter are clearly multi-annual.

This is perhaps **the main aspect that suggests the need for a different and innovative method of economic and accounting evaluation for these therapies**. In particular, these therapies produce **both direct and indirect long-term benefits**: increase in life expectancy, improvement in the quality of human life, treatment and stabilisation of various medical conditions (with an obvious impact on the value of human life); but also in terms of savings in treatment, in the consumption of pharmaceuticals and different types of health services; in terms of less use of hospitals, by improving the health of patients; in terms of costs related to the reduction of occupational activity; in terms of increased productivity, to the point of reducing the burden on families and health facilities to care for patients; the possibility, after the remission of the illness, of being able to continue to study and participate in community life; the positive effects on patients' job prospects; the longer time to potential pension burdens; the saving of resources consumed directly in healthcare facilities and that of family resources and direct and indirect care, increased productivity and higher tax revenues. These benefits must be assessed carefully and require the use of adequate financial and economic techniques[20]. On a methodological level, the literature regarding the estimation of these benefits, in terms of a reduction in the cost reduction or net present value, provides widely accepted indications.

The decision as to which therapy is worthy of funding should be based, as

20 *See Jorgens-Kefalas (2017), Ciarametaro at al. (2018), Duke-Margolis Center for Health Policy (2019), Salzman et al. (2018), Maes at al. (2019).*

far as is possible, on the estimation of the overall economic effects on the health service as a whole and on the health of citizens, not only considering the obvious upfront and immediate costs, but also the long-term value that they produce for society[21]. Therefore evaluating the current expenditure dimension but also the undoubted investment element of this type of therapy.

In this context, the usual economic and accounting evaluation approach, based on the estimation of the costs of conventional medicinal products and therapies (which are repeated and make provision for an annual treatment cycle) and on the accrual criterion typical of financial statements, is ill-suited to Advanced Therapy Medicinal Products and their technological and industrial characteristics. They require a novel health, economic, accounting and public finance approach. The effectiveness of these therapies must be verified over several years, when the more or less positive effects that they have had on the protocols for the care and treatment of the various conditions and on patients' quality of life and therefore the considerable savings in direct and indirect costs they afford, can be understood and estimated.

In economic analysis and effectiveness assessment terms, **Advance Therapy Medicinal Products clearly represent a new challenge for public health systems.** It is question of understanding which therapies will be possible, given the resources available, how to adopt them and according to which administrative, financial and accounting process – in particular, the methods and procedures for reimbursement, which must be suited to the health essence of these therapies[22].

21 *See ACI (2019).*

22 *In recent years, various gene therapies have become established and widespread in advanced countries, reflecting the development of healthcare protocols. They are evidence of the profound transformation of advanced medical research that is increasingly based on DNA and cellular modification. There are currently 6 gene and cell therapies considered by the regulatory authorities (EMA and AIFA). It is anticipated that within 5 years the number of these medical protocols could reach more than 60 specific gene therapies. These treatments have special and innovative characteristics: they no longer involve multiple treatments and repeated cycles, rather the harvesting of the patient's DNA, its genetic modification and one-shot remission in the patient.*

For the time being, the number of patients and the pool of potential candidates are still limited, essentially due to the rarity of the diseases treated or that can potentially be treated with these therapies. Once they are fully deployed, with a very high number of medical conditions and an increase in demand, the question of access to these types of treatment will be a hot topic. Public entities will therefore have to decide which and how many therapies to take on, how to fund them, which criteria to use to understand the effectiveness of the therapies, and lastly the inevitable moral dilemma of who to grant access to the therapies and according to what criteria and conditions.
It is therefore clear that **ensuring patients access to Advanced Therapy Medicinal Products will require the definition of an innovative approach to pricing and reimbursement practices, and a review of medical treatment reporting mechanisms. Accounting procedures that are as fair as possible and are shared** by the State and pharmaceutical companies must be identified, in order to increase patient access opportunities, but above all to allocate the cost of therapies and their benefits efficiently and fairly over time, in economic and accounting terms.
The question that interests public finance and accounting is how to evaluate Advanced Therapy Medicinal Products in economic and accounting terms. Current budgetary procedures are somewhat restrictive and rely on the principle of accrual budgeting and expenditure commitments – **the cost of a medicinal product must be reported in full in the budget for the financial year, based on the expenditure commitments defined**.

Questions to be answered for the classification of Advanced Therapy Medicinal Products (ATMPs) in national accounts

The question to be answered concerns the **possibility of classifying (wholly or in part), as well as the reasons behind this classification, public expenditure for the acquisition of ATMPs as** investments (unlike conventional medicinal products). More specifically, the possibility of classifying them as **gross fixed capital formation**.
To this end, after referring to the definitions of investment used in the national income statement systems by ISTAT (Italian Institute of Statistics), the European Union and the international community in general, **this chapter**

will specifically assess each of the conditions that make it possible to provide this answer. More specifically:

- the classification or ATMPs as tangible or intangible assets;
- the evaluation of ATMPs as a result of a production process;
- the continuity of their use over time;
- the conditions under which they can be defined as an intangible component of investment.

Does expenditure for the purchase of ATMPS represent gross fixed capital formation for the public administration?

In national accounting, investment i.e. the purchase of tangible and intangible assets and the building up of inventories is known as *Gross Capital Formation* (GCF). When the building up of inventories (or 'changes in inventories') is excluded, leaving only purchases of tangible or intangible assets, the result is known as *Gross Fixed Capital Formation* (GFCF).

Gross fixed capital formation measures total expenditure for 'products intended for use in future production'. They are therefore 'products that can be reused several times in production processes'. These types of product are known collectively as 'fixed' capital. Why not call them simply investment, as economists often do? Because the word 'investment' in everyday usage applies as much to financial investments as it does to investments in machinery and buildings. Therefore, in order to make a clear distinction, national accountants use this rather peculiar terminology. Lastly, the word 'gross' indicates that the expenditure is measured without deducting the consumption of fixed capital (wear and tear).

As regards the inclusion of tangible and intangible assets, the definition of gross fixed capital formation used in national and EU accounting reveals a broadening of the narrow vision of investment as a mere increase in physical and technological capital.

In national accounting, gross fixed capital formation is defined as the acquisition, net of disposals, of fixed capital, consisting of tangible and intangible assets. **Tangible assets include machinery, plant, equipment, furniture, means of transport, construction and buildings, and land. Intangible assets include software, patents, professional appointments for investment, etc**.

The definitions of gross fixed capital formation according to ISTAT, the international system of national accounts (SNA 2008) and scientific literature (Lequiller and Blades, 2004) are provided in the relevant appendix. This appendix also provides the definitions of intangible assets according to the OECD, the *Office for National Statistics* (ONS, UK) and the *International Public Sector Accounting Standard Board* (Ipsas 31).

Are Advanced Therapy Medicinal Products (ATMPs) tangible or intangible assets[23]?

As mentioned previously, ATMPs are biological medicinal products that are classified into four main groups:

- **Gene therapy medicinal products**: contain or consist of a recombinant nucleic acid able to induce a therapeutic, prophylactic or diagnostic effect. Gene therapy medicinal products make it possible to regulate, repair, replace, add or delete a genetic sequence. In the case of genetic diseases in which a gene is defective or absent, gene therapy consists in transferring a functioning copy of the gene in question.
- **Somatic cell therapy medicinal products**: contain or consist of cells or tissues that have been subject to substantial manipulation to change their biological characteristics, physiological functions or structural characteristics or that are intended to be used for the same original functions in the body. The purpose of somatic cell therapy is to treat, prevent or diagnose disease. The cells or tissues can be of autologous origin (derived from the patient him/herself), allogeneic (obtained from a donor) or xenogeneic (derived from a donor of an animal species other than man).
- **Tissue-engineered medicinal products**: contain cells or tissues that have been subjected to substantial manipulation or that are intended to be used for the same original functions in the body, in order to repair,

23 *"An intangible asset is by definition an asset without physical substance […] They cannot be held in the hand, or tagged with an inventory system" (EPSAS, 2018). More specifically, "an intangible asset is an identifiable non-monetary asset without physical substance" (IPSAS 31).*

regenerate or replace human tissues.

- **Combined advanced therapy medicinal products**: contain one or more medical devices as an integral part of the cell- or tissue-based medicinal product.

They are, therefore, **made up of genetic materials or cells or tissues or combinations thereof**, which are:

A often, by their very nature, **absolutely indistinguishable** from the cells and/or tissues of the patient or;

B absolutely **no longer detectable** as in the case of gene therapies for certain organs (retina of the eye, cochlea of the ear, etc.), since it is not medically possible, as well as being ethically incorrect, to subject a patient to retinal or cochlear sampling for follow-up, or

C **detectable only after highly invasive procedures**, e.g. bone marrow harvesting or skin or muscle biopsies, which are potentially life-threatening for the patient as well as being very costly. It would in fact be a case of characterising by gene sequencing or other 'omics' technologies (transcriptomics, proteomics, metabolomics, etc.), individual cells or tissues so as to distinguish the natural cells or tissues of the patient from those treated with ATMPs.

Let us not forget that **ATMPs also include personalised 'algorithms'**, and even more specific and in many cases individualised procedures such as *genome editing* in which the correction of the gene defect is specific to an individual subject and takes place through a completely personal biotechnological procedure.

So, are they tangible or intangible assets? They are certainly goods produced thanks to scientific research in order to cure disease and that therefore have long-term effects on health, people's well-being, productive potential and healthcare costs.

However, in the light of the foregoing, it is clear that with respect to the current distinction between tangible and intangible assets, **ATMPs fall within the second category as their 'physical' substance is only in some limited cases identifiable over time and moreover using costly, invasive proce-**

dures that are often harmful to the patient's health.
Regardless of how ATMPs are qualified as assets, **in order for them to be recognised in gross fixed capital formation, the following two requirements must be fulfilled**.

Are ATMPs the product of production processes?

ATMPs are products of complex productive processes, characterised by a substantial research component. In actual fact, they consist of 'live' drugs whose safety and quality is guaranteed by production processes that are very different to those used for conventional medicinal products, which are based on chemical synthesis. For example, ATMPs cannot be sterilised, because this process would destroy the product. It is precisely this innovative nature that makes their production a very complex sector requiring high-quality manufacturing sites able to operate in strict compliance with GMP (*Good Manufacturing Practice*). **The first requirement for being able to consider ATMPs capital assets can therefore be considered fulfilled**.

Are ATMPs used repeatedly or continuously in these same processes for more than one year?

ATMPs include both medicinal products in which the production process consists of a first phase in the laboratory (*in vitro*), and a second phase inside the body (*in vivo*), and medicinal products that are directly applied *in vivo* inside the human body In both cases they exert their action continuously over time and with characteristics customised to suit the patient. The second requirement for being able to consider ATMPs capital assets could be considered fulfilled.

One distinctive aspect of ATMPs, in which they differ them from the vast majority of conventional medicinal products is that, after transfection in the body, the subsequent phase of the production process takes place inside the body and continues over time.

This is the characteristic **that allows ATMPs to maintain their curative action and bring about a permanent or in any case very long-lasting improvement in people's health and therefore personal and professional lives**. The most recent data already show the persistence of the therapeutic effects of

those ATMPs whose clinical trials and therefore patient enrolment started approximately 20 years ago.

As a bridge improves mobility between territories and can be used over time, scientific research increases knowledge wealth and allows further progress, and expenditure for defence systems improves citizens' safety for an extended period, ATMPs improve living conditions, generate substantial direct and indirect savings for the NHS and people's productive potential, if not permanently, certainly for an extended period of time (at the current state of knowledge many decades).

If ATMPs were classifiable as intangible assets[24], would the other requirements established by IPSAS 31[25] be fulfilled?

- *Identifiability.* Is the asset identifiable, i.e. is it separable (can it be sold, transferred, rented, licensed or exchanged) or does it arise from legal or contractual rights[26]?

  Identifiability does not necessarily imply transfer but may arise from contracts or legal rights. In the case of ATMPs, identifiability arises from contractual rights. In fact, when the NHS purchases an ATMP, it signs a purchase agreement that is conditional on its effectiveness. The NHS pays the installment if the medicinal product works, therefore the property rights over that medicinal product are transferred to the NHS only if the effects of the medicinal product last for an extended period. The

24 *See the Appendix A for the definition.*

25 *See the Appendix A for the definition.*

26 *From IPSAS 31. An asset is identifiable if it either:*

a) Is separable, i.e., is capable of being separated or divided from the entity and sold, transferred, licensed, rented, or exchanged, either individually or together with a related contract, identifiable asset or liability, regardless of whether the entity intends to do so; or

b) Arises from binding arrangements (including rights from contracts or other legal rights), regardless of whether those rights are transferable or separable from the entity or from other rights and obligations. For the purposes of this Standard, a binding arrangement describes an arrangement that confers similar rights and obligations on the parties to it as if it were in the form of a contract.

NHS only buys the durable part of the medicinal product, not the whole medicinal product.

- *Control of the asset by an entity*[27]. The NHS currently controls both the production of ATMPs (i.e. through audits by Competent Authorities – the AIFA in Italy – in order to apply Good Manufacturing Practice (GMP), which is mandatory under Italian Law 219/2006 as amended), and the acquisition of ATMPs, i.e. it has the power to obtain future economic benefits or service potential flowing from the underlying resource and to restrict the access of others to such benefits or service potential.
- *Future economic benefits and service potential*[28]. It is probable that future economic benefits or service potential will flow to the entity. The requirement is fulfilled, from the NHS perspective.
- *The value of benefits can be reliably estimated*[29]. This requirement is also fulfilled as the benefits can be identified and quantified and the cost value of ATMPs can be reliably evaluated.

Can public expenditure for the purchase of ATMPs be classified as gross fixed capital formation?

On the basis of the above considerations, **there seems to be sufficient grounds for including ATMPs as an intangible component of gross fixed capital formation**.

27 *From IPSAS 31. Control of an Asset. An entity controls an asset if the entity has the power to obtain the future economic benefits or service potential flowing from the underlying resource and to restrict the access of others to those benefits or that service potential. The capacity of an entity to control the future economic benefits or service potential from an intangible asset would normally stem from legal rights that are enforceable in a court of law. In the absence of legal rights, it is more difficult to demonstrate control. However, legal enforceability of a right is not a necessary condition for control because an entity may be able to control the future economic benefits or service potential in some other way.*

28 *From IPSAS 31. The future economic benefits or service potential flowing from an intangible asset may include revenue from the sale of products or services, cost savings, or other benefits resulting from the use of the asset by the entity.*

29 *From IPSAS 31. The cost or fair value of the asset can be measured reliably.*

Besides, the scope of intangible assets is subject for study and discussion by national accountants at international level. At European level, several working groups promoted by Commission and Eurostat have been set up to analyse expenditure for intangibles, environment-related expenditure and the accounting treatment of social benefits.

What is the value of ATMPs that could be accounted for? The cost-side approach or the expected net economic value (NEV)? How can it be accounted for over time in line with the time distribution of their effects?

AS evidence of the consideration of **future economic benefits as an estimate of the increase in the value of the capital stock from intangible assets**, in the 2010 ESA Regulation, it is stated that the "*value of expenditure on creative work undertaken on a systematic basis in order to increase the stock of knowledge, including knowledge of man [...] is determined in terms of the economic benefits expected in the future. Unless the value can be reasonably estimated it is, by convention, calculated as the sum of costs, including those of unsuccessful research and development. Research and development that will not provide a benefit to the owner is not classified as an asset and is instead recorded as intermediate consumption (AN1171)*".

The estimation of the net economic benefits of ATMP can therefore benefit from the wealth of literature on methods for estimating the effects of health investments on population well-being and income generated.

7. Some open fronts in the development of the national accounts system: well-being, the environment and human capital

Environment

The increased availability of statistics on environmental goods and flows has led to the development of accounts in order to trace, in an integrated and coherent manner, the various elements of the environment and how they are linked to the economy. In 2012, the United Nations Statistical Commission published a new System for Environmental-Economic Accounting

(SEEA) and adopted the core structure of this system as the international standard. The SEEA proposes a framework for measuring environmental resources in both physical and monetary units. The elements of the SEEA core framework are currently being implemented in many countries worldwide. Within the European Union, a first EU regulation on environmental accounts adopted in 2011 requires all Member States to compile annual data on three modules: environmental tax; air emissions of 14 substances; and material flow accounts. A second EU regulation includes three new modules on: expenditure for environmental protection; environmental goods and services; and physical energy flows. Other types of capital besides natural resources are considered for sustainability.
In order to take into account the broad range of indicators required to measure sustainable development, in 2015, the United Nations adopted Agenda 2030 (Sustainable Development Goals, SDGs). At present, environmental issues are integrated into national accounting by means of satellite accounts.

Well-being, *GDP and Beyond*

The issue of moving beyond the GDP as a measurement of societal progress has been discussed at international level for many years now. In the early 1990s, the United Nations created the human development index (a synthetic indicator of progress based on three factors: production, education and health).
Since 2001, the OECD has promoted several projects aimed at raising awareness concerning the measurement of societal progress and individual well-being. With the OECD Istanbul declaration, which was adopted by the major international organisations in June 2007,
international consensus on the need to measure societal progress by going beyond conventional economic measurements such as GDP per capita was achieved for the first time.
In 2010, the European Commission published: "GDP and beyond. Measuring progress in a changing world", also taking into consideration the Report by the Stiglitz-Sen-Fitoussi Commission promoted by the French government.
Since the launch of the Europe 2020 Strategy for Smart, Sustainable and Inclusive Growth in 2010, there has been a rapid increase in the importance

of statistics on income and living conditions. And in 2011, the ESS adopted the final report of the Commission on the Measurement of Economic Performance and Social Progress, otherwise known as the Stiglitz-Sen-Fitoussi Commission (Stiglitz *et al*., 2009).

Lastly, the beyond the GDP debate and Agenda 2030 on SDGs have drawn attention to the need to integrate GDP measurements with indicators that include the social and environmental aspects of progress.

The need to produce statistics on the different dimensions of well-being to accompany conventional economic development measurements has also emerged in the national accounting setting.

For example, in the recitals of the 2010 ESA Regulation, in addition to the question of environmental and social accounts, there is a commitment to supplement the system of accounts with new well-being and progress measurements. "*In the case of environmental and social accounts, the Communication from the Commission to the Council and the European Parliament 'GDP and beyond – Measuring progress in a changing world', should also be fully taken into account: […] There is a need to vigorously pursue methodological studies and data tests, etc. with the aim of developing a more comprehensive measurement approach for wellbeing and progress. This should allow data that complement GDP aggregates to be made available as soon as possible. Data on national and regional accounts should be seen as one means of pursuing those aims*".

It is important to point out that health represents one of the components systematically included in all conceptual frameworks of well-being that have been developed by international institutions and organisations, as well as by the individual Member States. In a recent ISTAT sample survey on the importance citizens give to the 12 components of fair and sustainable well-being, health occupied first place (ISTAT, 2018).

As further proof of the relevance of health also at the institutional level, in Italy 12 indicators of fair and sustainable well-being have been included in the budget planning documents (DEF) and budget law since 2016. These include the measurement of **healthy life expectancy** (as well as an indicator measuring excess weight). Citizens will therefore have to be informed of the goals set and the results achieved also regarding these topics.

8. Current accounting criteria and the application of Annuity Payment Models for ATMPs

The **net balance to be financed**, which is calculated on a **legal (financial) accrual** basis, equates at the forecast stage with expenditure authorisation, i.e. the appropriation provided for by specific legal provisions, and in the management stage with the accounting commitment.

Net borrowing, on the other hand, is calculated on an **economic accrual** basis, a principle that in this case (as the expenditure relates to gross fixed capital formation) **conventionally**, for the reasons described below, applies the cash criterion; this criterion is also valid for **requirements**; i.e. reference is made to the actual annual disbursements expected to be made for the implementation of the intervention, although, as far as borrowing is concerned, in accordance with the 2010 SEC, gross fixed capital formation is recorded at the time when ownership of the assets is transferred to the institutional unit that intends to use them and consequently the amount to be recorded corresponds to the actual increases/decreases in the value of the investment asset.

Moreover, it was agreed that – due to the lack of information on the actual time at which the aforesaid effect is produced – the recording of investment in net borrowing should be based, conventionally, on actual payments, because they are more representative of the increase in capital stock in the period considered than the accounting commitment.

Therefore, the conventional criterion applied for fixed capital formation, by virtue of which the impact on net borrowing is represented by the payments made on the basis of the state of progress, i.e. on the part of the work or intervention completed, can also be extended to expenditure for Advanced Therapy Medicinal Products with the same impact on net borrowing and requirements, corresponding to the payments in relation to the benefits of the therapy the patient undergoes.

Without prejudice to the general principles referred to above, it is first and foremost appropriate to observe that **the accounting systems of State, Regional and Local Health Authorities are different in nature and are governed by different regulations**.

For the **State and Regional Authorities**, the main accounting system is **financial ac-**

counting, which is based on the financial accrual and cash principles. The financial accrual principle provides for and guides the forecasting, detection and reporting of assessments and commitments, whereas the cash principle provides for and guides the forecasting, detection and reporting of receipts and payments.
For **public health authorities**, on the other hand, the main accounting system is **economic and financial accounting**, based on the accrual principle, resulting in a balance sheet presenting assets, liabilities and, by their difference, net worth, as well as in an income statement presenting incomes, expenses and, by their difference, the economic result for the year.
The **accrual** principle also forms the basis of the **consolidated balance sheet of Regional Health Services**, which derives from the consolidation of the balance sheets of all the public health authorities in the Region and the centralised Healthcare Administration (GSA) within the Regional Authority (article 32 of Italian Legislative Decree 118/2011). The consolidated data of Regional Health Services are particularly relevant because they form the basis for the annual auditing of regional healthcare accounts and for the possible preparation of coverage pursuant to article 1(174) of Italian Law no. 311/2004.
The financial accounting systems are, in turn, governed by different standards.
The **Regional Authority system** is governed by **Italian Legislative Decree no. 118/2011** ("Provisions on the harmonisation of the accounting systems and budget schemes of the Regional and Local authorities and their bodies, in compliance with articles 1 and 2 of Italian Law no. 42 of 5 May 2009), with different rules for the ordinary management of the Region (Titles I and III) and health management (Title II, setting out the 'General and applied accounting standards for the health sector"').
The **Central Government system** was reformed by **Italian Law no. 196/2009** ('Public Finance and Accounting Law'), which was followed by the issuance of several relevant Legislative Decrees, amongst which Italian Legislative Decree 93/2016 ("Reorganisation of the regulations governing budget management and the strengthening of the cash budget function, pursuant to article 42(1) of Italian Law no. 196 of 31 December 2009") is particularly relevant in terms of **possible Annuity Payment Models**, and specifically refers to the new definition of accounting commitment.
One particularly significant innovation of **Italian Legislative Decree 118/2011** regarded the review of the concept of financial accrual with the introduction

of the **'enhanced financial accrual'** principle. On the basis of this principle (annex 4/2, point 2), "*perfected legal obligations are recorded in accounting records when the obligation arises, charging them to the year in which the obligation expires. The expiry of the obligation is the moment in which it becomes due. The established case-law of the Italian Court of Cassation defines a credit as being due when no obstacles to its collection and it is therefore permissible to demand fulfilment*". More specifically, as far as commitments are concerned (article 56(1)), "*all legally perfected obligations payable, from which expenditure is incurred for the Regional Authority, shall be entered in the accounting records when the obligation is perfected, and charged to the financial year in which the obligation expires, in accordance with the approach provided for by the principle applied to financial accounting referred to in annex no. 4/2*".

The enhanced financial accrual principle is therefore fully consistent with an Annuity Payment Model, which could be applied by the NHS for the purchase of ATMPs, in that it provides that the **commitment of expenditure for purchases is made at the moment in which the legal obligation is fulfilled, but is charged to the financial years in which it is expected the corresponding payments will be made, in accordance with the contractually established due dates**.

For Central Government, legislation based on the enhanced financial accrual principle has since been introduced. More specifically, Italian Legislative Decree 93/2016 (article 3) replaced article 34 of Italian Law no. 196/2009 introducing, starting from financial year 2019, "*the new concept of multi-year commitment 'upon collectability', based on which accounting commitments must be assumed, within the limits of the appropriations entered in the multi-year budget, with the expenditure charged to the financial years in which the obligations fall due (i.e. when they expire)*" (Senate Research Service, Dossier no. 413, July 2021, page 10).

Lastly, a more conventional definition of commitment persists for **regional healthcare management**, according to which "*the Regional Authorities: a) assess and commit during the financial year the full amount for current health funding, including the bonus share conditional to the verification of regional fulfilments, and the shares of health funding that are tied or finalised (article 20(2) of Italian Legislative Decree 118/2011)*". This definition of commitment is consistent with an *Annuity Payment Model* only to the extent that, as a result of the application by the Central Government of the new definition of

accounting commitment, the transfers from the Central Government that finance the expenditure (for example, the purchase of ATMPs) are assessed by the Regional Authority in installments, which therefore also entails payment of the corresponding commitments on an installment basis. This could also result in an inconsistency between the transfers assigned to the public health authorities and the costs detected by them (infra).

An *Annuity Payment Model* contractually established between manufacturers and the Italian Medicines Agency would fit perfectly with the economic characteristics of ATMPs. Indeed, as discussed in the paragraphs above, the cost of Advanced Therapy Medicinal Products is substantial and concentrated in the short term, whereas their effectiveness and corresponding benefits for patients cover a far broader time horizon. Consequently, agreements between the public payer and the manufacturers of Advanced Therapy Medicinal Products to ensure that the accounting commitment follows the payment due date, i.e. the cash criterion, are to be considered plausible. In this way, the timescale of the authorisation of expenditure borne by the public budget would be substantially in line with that of the effects in terms of the therapeutic benefits for patients.

In this payment model, **potential disbursements for ATMPs are linked to the success of the therapies and it therefore appears completely logical that accrual, by analogy with tax credits** (see chapter 2), can largely follow the tax criterion. In actual fact, with the *payment at result mechanism*, **the certain public commitment is only associated with the first installment of the cost of the therapy, which can therefore, be committed as a certain expense. The subsequent installments and disbursements, being distributed over a later period of time, could, like tax credits** (see chapter 2), **follow the cash criterion**.

To this overall end, it would appear appropriate, although not strictly necessary, to introduce a specific provision that would charge the expenditure commitment for the purchase of ATMPs, accrued over several years and conditional on the result, to the years in which it is expected the payments are to be made according to the due dates contractually established in the payment models negotiated between the manufacturers and the Italian Medicines Agency.

As regards the public health authorities, their economic and financial accounting is primarily governed by the provisions of the Italian Civil Code as a result of the reference made by article 28 of Italian Legislative Decree no.

118/2011: "*For the preparation of the financial statement, the entities referred to in letters b) point i), c) and d) of subsections 2 of article 19 shall apply articles 2423 to 2428 of the Italian Civil Code, with the exception of those aspects otherwise provided for in this title*". The main exceptions to the Civil Code rules are set out in article 29 (Evaluation principles specific to the health sector"). With specific reference to ATMPs, the practice whereby "*in order to apply the PAR (payment-at-results) payment model, for income statement accounting, the user centre must proceed with allocation in accordance with the invoicing time-points provided for when the different clinical results are achieved, as per the negotiation agreements between the Italian Medicines Agency and the pharmaceutical company, also to avoid charging the full cost of the purchased medicinal product and in order to further ensure alignment with the various information flows*" (ALISA Resolution no. 216 of 21/6/2021) has recently become widespread, at least in some regions and by explicit regional indication. This practice ensures the consistency of the values recorded at the different institutional levels. At present, however, it does not find specific regulatory cover in Italian Legislative Decree 118/2011.

It would therefore appear necessary to introduce a specific regulatory provision whereby the entities referred to in article 19(2), letter b) point i) and letter c) of Italian Legislative Decree 118/2011 must allocate the costs incurred to purchase advanced therapy medicinal products over the financial years in which it is expected the corresponding payments will be made in accordance with the due dates contractually established in the negotiation agreements, in an amount corresponding to such payments. In this case, the same requirements shall apply to the consolidated financial statements of the Regional Health Service pursuant to article 32 of Italian Legislative Decree 118/2011.

Introducing the accounting changes suggested in this chapter for an effective implementation of an Annuity Payment Model for ATMPS would actually result in an alignment between cash, financial accrual and economic accrual, consequently generating 'good debt' as is the case for investment. Although, on the one hand, this effect would help – as already described at length – healthcare facilities/prescribing centres to effectively apply *at result* payment models and would help the NHS to dilute expenditure for ATMPs over time in line with the expected benefits, on the other hand, the difficulty for the authorities

in being able to quantify expenditure for the purchase of ATMPs *ex ante* and control the deficit generated *ex post*, could result in them adopting a closed attitude to this proposal, despite the validity of the underlying principles.
In order to overcome this barrier and allow for a timely programming of expenditure for ATMPs and the subsequent monitoring of the expenditure by the relevant authorities, it is deemed that it might be decisive to introduce the accounting change discussed in this chapter within the framework of a specific multi-year expenditure authorisation, by setting up an *ad hoc Fund* for ATMPs with these accounting characteristics. Such a Fund could make provision for the allocation of determined sums (thus satisfying expenditure planning and monitoring requirements) and allow for a more appropriate evaluation of the distribution of benefits on a multi-year level within the framework of a controlled management of the expenditure.
Another important point is that the use of a budget impact analysis would appear able to offer interesting prospects. This approach must, however, be synchronised with the budget of the health services – and public budgets more generally – which are based on annual expenditure commitments. In the case of ATMPs, it is therefore necessary to adopt an approach based on the time horizon of the economic and financial impact of the different expenditure items, which is multi-year. It is necessary to find an appropriate balance between the annual dimension of budgets and the accrual of costs and benefits in the health sector, which clearly exceeds the exclusive dimension of one year[30].

30 *"Budget impact analyses should be presented for the time horizons of most relevance to the budget holder. They should accord with the budgeting process of the health system of interest, which is usually annual. The framework should allow, however, for calculating shorter and longer time horizons to provide more complete information of the budgetary consequences. A particularly useful extension of the time horizon for a chronic health condition is to reflect the impact that might be expected when a steady state would be achieved if no further treatment changes are assumed. This will vary with the condition and with the impact of the new intervention but will generally be longer than the current budget period because of costs and benefits that accrue over time. Although time horizons that go beyond a few years are subject to considerable assumptions, they may in exceptional cases be required to cover the main implications of the health condition (e.g., some vaccinations). In any case, results should be available disaggregated over time in periods appropriate to the budget holder (e.g., annual, etc.). Hence, to be most useful, the output must be the period by period level of expenses and savings rather than a single 'net present value'" Mauskopf et al. (2007).*

Conclusions

ATMPs represent a revolution for the treatment of complex diseases with no alternative treatment options, with clinical and economic characteristics that differ from conventional medicinal products and that can result in substantial cost savings for the NHS.

This paper has argued that it is already possible to measure the benefits over time and the savings for the NHS generated by ATMPs. Therefore, applying the conventional criterion used for gross fixed capital formation, by virtue of which the impact on net borrowing is represented by the payments made on the basis of the state of progress, can also be extended to expenditure for Advanced Therapy Medicinal Products with the same impact on net borrowing and requirements, corresponding to the payments in relation to the benefits of the therapy the patient undergoes. Hence, the potential for using Annuity Payment Models conditional on the result (*payment at result*) for the purchase by the NHS of Advanced Therapy Medicinal Products that allow it to spread the high costs of these therapies over time in step with the expected benefits, by applying the accounting criteria suggested in chapter 8, **so that legal accrual follows economic accrual**. In addition, in order to allow the competent authorities to quantify *ex ante* expenditure for the purchase of ATMPs and to *ex post* monitor the burden generated for public finance, the accounting criterion referred to in chapter 8 could be applied within the framework of a **multi-year *ad hoc* revolving Advanced Therapy Medicinal Products fund** that could provide for the **advance allocation of determined sums** and allow a more appropriate multi-year assessment of the **distribution of the benefits.**

Such a dedicated ATMP fund can be financed with an increasing initial endowment up to the fifth year (maximum duration of the installment facility) based on the accounting principle referred to in chapter 8, when the greatest impact of the installment facility should be recorded. From the fifth year, the endowment should remain unchanged, since the number of further installments associated with new contracts should be offset with: (I) the outgoing installments of expired contracts; (II) any installments not paid due to failure by the administered therapy to achieve the expected results; (III) the economic benefits measured in terms of the savings for the National Health Service; and (IV) the surplus of the previous accrual year, where applicable.

Appendix A
EU Accounting Rules

A EU Accounting Rules for therapies/medicinal products

The ESA10 establish that: "*social transfers in kind are accounted as consumption expenditure. These are individual goods or services*:

a *in the form of reimbursements by social security funds of approved expenditures made by households on specific goods and services; or*

b *provided directly to the beneficiaries by market producers from which general government purchases the corresponding goods and services".*

Examples of social transfers in kind are medical or dental treatments, surgery, hospital accommodation, spectacles or contact lenses, medical appliances or equipment, and similar goods or services meeting social risks or needs (p. 113 par. 4.110 ESA10).

Based on the above principle, the regulations for the preparation of the national budget require for the cost of a medicinal product or therapy to be recorded in full (apart from the payment flow) in the financial statement, on the basis of defined budget commitments and the accrual method of allocation. Such expenditures can also be settled and paid in subsequent years, **however the total amount must be recorded in the year in which it is committed**.

B Gross fixed capital formation

In national accounting, investment i.e. the purchase of tangible and intangible assets and the building up of inventories is known as *Gross Capital Formation* (GCF). When the building up of inventories (or 'changes in inventories') is excluded, leaving only purchases of tangible or intangible assets, the result is known as *Gross Fixed Capital Formation* (GFCF). This aggregate measures total expenditure for 'products intended for use in future production'. They are therefore 'products that can be reused several times in production processes'. These types of product are known collectively as 'fixed' capital. Why not call them simply investment, as economists often

do? Because the word 'investment' in everyday usage applies as much to financial investments as it does to investments in machinery and buildings. Therefore, in order to make a clear distinction, national accountants use this rather peculiar terminology. Lastly, the word 'gross' indicates that the expenditure is measured without deducting the consumption of fixed capital (wear and tear).

Inclusion of tangible and intangible assets: the definition of gross fixed capital formation used in national and EU accounting reveals a broadening of the narrow vision of investment as a mere increase in physical and technological capital.

In national accounting, gross fixed capital formation is defined as the acquisition, net of disposals, of fixed capital, consisting of tangible and intangible assets. **Tangible assets include machinery, plant, equipment, furniture, means of transport, construction and buildings, and land; intangible assets include software, patents, professional appointments for investment, etc.** It is important to point out once again that within the logic of national accounting these assets have the common characteristic of representing the product of production processes and they are used repeatedly or continuously in these same processes for more than one year. The increases in value of non-produced tangible assets add to the acquisition of fixed assets.

- *ISTAT definition.* Gross fixed capital formation consists of the acquisitions (net of disposals) of fixed assets by resident producers, plus the increases in value of non-produced assets (e.g. land). Fixed assets consist of produced tangible and intangible assets (e.g. software), that are intended to be used in production processes for a period exceeding one year.
- *2008 SNA definition.* Fixed assets are produced assets that are used repeatedly or continuously in production processes for more than one year.
- *Definition of Lequiller, Blades, 2014.* Gross capital stock is the value of all fixed assets still in use, at the actual or estimated current purchasers' prices for new assets of the same type, irrespective of the age of the assets. Net capital stock is the sum of the written-down values of all the fixed assets still in use; it can also be described as the difference between gross capital stock and consumption of fixed capital.

C Intangible fixed assets

- *OECD definition.* Intangible fixed assets are non-financial produced fixed assets that mainly consist of mineral exploration, computer software, entertainment, literary or artistic originals intended to be used for more than one year.
- *Definition of the Office for National Statistics (ONS), UK.* Intangible fixed assets include mineral exploration, computer software and entertainment, and literary and artistic originals. Expenditure on them is part of gross fixed capital formation. They exclude non-produced intangible assets such as patented entities, leases, transferable contracts and purchased goodwill, expenditure on which would be intermediate consumption.
- *IPSAS 31 definition.* An important contribution to the definition of intangible assets is made by the International Public Sector Accounting Standard Board (IPSASB) of International Financial Reporting Standards (IFRS) Foundation. According to IPSAS 31, an asset should be recorded as intangible if, and only if, it satisfies all of the following criteria:
  - it is identifiable, i.e. is it separable (can it be sold, transferred, rented, licensed or exchanged) or arises from legal or contractual rights;
  - the public sector entity has current control over it, i.e. it has the power to obtain the future economic benefits or service potential flowing from the underlying resource and to restrict the access of others to those benefits or that service potential;
  - it is probable that future economic benefits or service potential will flow to the entity;
  - cost or fair value of the asset can be measured reliably.

The separability requirement represents a critical point for the recognition of human capital as a public resource. Increasing the skills of the population can be equated with improving the state of health.

D Indirect investments

- *OECD definition.* Indirect investments are capital expenditures that constitute investment grants and transfers to other subjects (businesses,

households and private social institutions, abroad) provided unilaterally without any *quid pro quo*.

- *SNA definition.* Investment grants consist of capital transfers in cash or in kind made by governments to other resident or non-resident institutional units to finance all or part of the costs of their acquiring fixed assets.

E Investment in knowledge

- *OECD definition*. Investment in knowledge is defined as the sum of expenditures in research and development (R&D), on total higher education (public and private) and on software. It includes current expenditures, such as on education and R&D, as well as capital outlays, such as purchases of software and construction of school buildings.

F Human capital

- *OECD definition*. The OECD defines human capital as "the knowledge, skills, competencies and other attributes embodied in individuals or groups of individuals acquired during their life and used to produce goods, services or ideas in market circumstances" (Boarini *et al*., 2013).
- *United Nations definition*. Human capital is productive wealth embodied in labour, skills and knowledge.

G Human development

- *OECD definition*. Human development is the process of enlarging people's choices. Their three essential choices are to lead a long and healthy life, to acquire knowledge and to have access to the resources needed for a decent standard of living.

H Research and Development (R&D)

- *SNA definition.* Research and development by a market producer is an activity undertaken for the purpose of discovering or developing new products, including improved versions or qualities of existing products, or discovering or developing new or more efficient processes of production.
- *UNESCO definition.* Any creative systematic activity undertaken in order to increase the stock of knowledge, including knowledge of man, cul-

ture and society, and the use of this knowledge to devise new applications. Includes fundamental research, applied research in such fields as agriculture, medicine, industrial chemistry, and experimental development work leading to new devices, products or processes.

- *OECD definition.* Research and development is a term covering three activities: basic research, applied research, and experimental development (Frascati Manual). Research and development expenditure is the money spent on creative work undertaken on a systematic basis to increase the stock of knowledge and the use of this knowledge to devise new applications.

  Expenditure on R&D refers to all expenditure on research performed at universities and at other institutions of tertiary education, regardless of whether the research is funded from general institutional funds or through separate grants or contracts from public or private sponsors. This includes all research institutes and experimental stations operating under the direct control of, or administered by, or associated with, higher education institutions.
- *R&S and scientific and technological innovation OECD Definition (Frascati Manual).* Scientific and technological innovation may be considered as the transformation of an idea into a new or improved product introduced on the market, into a new or improved operational process used in industry and commerce, or into a new approach to a social service. The word 'innovation' can have different meanings in different contexts and the one chosen will depend on the particular objectives of measurement or analysis.

Appendix B
Accrual accounting, Cash basis accounting, Italian Decree 118

Current budgetary procedures are clear and do not generally provide for exceptions to the principle of accrual budgeting and expenditure commitments[31]. State budgeting rules provide that the total cost of a medicinal product or therapy must be reported in full in the budget for the year, based on the expenditure commitments defined. This expenditure may also be settled and paid in subsequent years, but the fact remains that its full amount must be charged in the year in which it arises. The accrual criterion identifies the criterion with which to change the costs and the effects of the assets of the various public administrations that occur in each year, regardless of financial and cash movements. The consequence of the transactions must be recorded in the accounting records and assigned to the financial year such transactions refer to, not to the financial year in which the corresponding financial movements occur (which are instead recorded in the cash budget).

The State budget and the budget of other public administrations are twofold: the **accrual budget** presents the legal obligations (expenditure commitments) created in a given year; whereas the cash budget records the actual expenditures (payments). The accrual principle requires transactions to be recorded in the period in which they arise, regardless of the time at which the payments are made. The **cash principle**, on the other hand considers only the expenses and income for which there has been a financial event (they gave rise to a movement of money). Income and expenditure entries must be recorded at the time when the conditions giving rise to the economic effects of the expenditure decision are fulfilled, i.e. when the commitment actually takes place, regardless of when the payment is made. This procedure and the annual nature of the state budget does not exclude

31 *See Italian Law no. 196 of 31 December 2009, which governs the criteria for the formation of the state budget, Italian Law no. 243 of 24 December 2012 and Italian law no. 163 of 4 August 2016, which updated and reviewed these criteria.*

that a payment spread over several years is not per se admissible[32].
A large part of expenditure on health is considered current expenditure. It goes without say that this is indisputable for may expenditure items – personnel, salaries, etc. However, increasingly obviously, more and more therapies and new health protocols are taking on the visible characteristics of investment expenditure. The spread of the COVID-19 epidemic made it blatantly obvious that health is a fundamental investment for any country and determines its sustainability and economic and social success. An increasing and substantial part of health expenditure has clear investment characteristics, in that it is able to produce benefits over a multi-year time-frame; it goes without say that this strong investment component of health expenditure is not easy to estimate. As indicated in the public accounting standards (see RGS 2019), investment expenditures identify all expenditures with a direct or indirect impact on the formation of national, physical and human capital and in terms of resources. In the current definition, public investment is represented by the "*volume of expenditure that the State, Regional Authorities and other Public Administrations support with the aim of increasing the stock of physical and technological capital available to the country*".
Italian Legislative Decree 118/2011 ('Decree 118') significantly innovated the financial and economic accounting rules of the Regional Authorities, Local Health Authorities, hospitals and research hospitals. This innovation was aimed at achieving greater control over public finance balances by central government by providing precise economic and financial rules for the

32 *As pointed out in RGS (2019), the resources allocated in the expenditure estimates are deployed in a four-stage process: commitment, settlement, ordering and payment. "The allocation of financial resources provided for by budget estimates have margins for flexibility that make it possible to combine the management and executive function with the authorising nature of the budget law. These margins are established by Italian Law no. 196 of 31 December 2009 and by other associated regulatory sources. In addition to by any new expenditure laws or rules establishing new levies that may be passed by Parliament during the financial year, the forecasts provided by the budget law may be modified with other regulatory or administrative instruments. The accounting and public finance law provides that the adjustment law is the regulatory approach for intervening in the budget during the financial year. The adjustment shows the values of the changes – compensatory, between programmes of the same mission – on an accrual and a cash basis, which can alter the forecasts for the current financial year only".*

preparation of balance sheets and the evaluation of expenditure and revenue. This step was essential in order to avoid situations of financial collapse of the decentralised authorities, especially in the health sector, which was characterised by large deficits and substantial budget imbalances.
Decree 118 clearly assimilates Local Health Authorities and hospitals to a private operator with the extension to these subjects of economic and financial accounting: in addition to the financial accounts, it provides for the preparation of an income statement, a balance sheet and a multi-year budget in order to provide a full account of the evolution of the budget of these entities and put the various budget items under the control of the Ministry of Economics and Finance. Provision was therefore made, albeit with a few exceptions, for the definitive assimilation of the budgets of Local Health Authorities and Hospital to the principles for balance sheet preparation imposed by the Civil Code. Precise rules were therefore introduced entailing precise and consistent real-time monitoring of the trends of the budget balances of healthcare entities and of their effects on public finance balances.
The provisions of Decree 118 also require the preparation of a consolidated balance sheet in order to ensure full consistency and the "reconciliation between the items entered and accounted for in terms of economic and financial accounting and those entered in terms of financial accounting".
Article 25 of Decree 118 explicitly makes provision for an annual economic budget forecast: "*1. The entities referred to in article 19(2), letter b), point i), where the conditions provided for therein exist, and letter c) shall prepare an annual economic budget forecast that is consistent with healthcare planning and with the economic and financial planning of the region. 2. The annual economic budget forecast shall include a forecast income statement and a projected cash flow plan, drawn up using the income statement and cash flow statement schemes provided for in article 26. The detailed income statement, drawn up in accordance with the EC scheme pursuant to the Italian Ministerial Decree of 13 November 2007, as amended, shall be appended to the income statement. 3. The annual economic budget forecast shall be accompanied by explanatory notes and the investment plan*".
Article 26 also provides for a financial statement and the budget schemes of the NHS entities: "*1. The financial year budget shall be drawn up with reference to the calendar year. It shall consist of the balance sheet, the income statement,*

the cash flow statement and the explanatory notes […]. 2. The financial statement prepared by the entities referred to under article 19(2) letter d) shall be submitted to the Board of Directors of the entity for approval. 3. In order to give a uniform structure to the items of the annual economic budget forecast and financial statement, as well as homogeneity to the values entered under such items, the entities referred to under article 19(2) letter c) and letter b) point i), where the conditions provided for therein exist, shall prepare the financial statement in accordance with the relevant schemes provided in annex no. 2, which constitute an integral part of this Legislative Decree. The entities referred to in article 19(2) letter d) shall adopt the sample financial statement schemes and adapt the explanatory notes and management report to the specific characteristics of their operational context".

The most essential point, however, comes in article 56 of Legislative Decree 118/2011, in which the aspect of greatest relevance for our analysis appears. The article provides that for expenditure commitments: "***1. All legally perfected obligations payable, from which expenditure is incurred for the Regional Authority, shall be entered in the accounting records when the obligation is perfected, and charged to the financial year in which the obligation becomes due, in accordance with the approach provided for by the principle applied to financial accounting referred to in annex no. 4/2****. Expenditures shall be entered in the accounting records, even if they do not result in actual cash movements. 2. The commitment constitutes the phase of expenditure with which the completion of a payable legal obligation is recognised, and the reason for the debt, the sum to be paid, the creditor, the specification of the constraint placed on budget appropriation and the due date shall be determined. 3. Expenditure commitments shall be assumed within the limits of the relevant appropriations of the budget and entered in the financial years in which the obligations fall due".*

Therefore an expenditure is actually committed only when the "legal obligation is perfected" and it is entered "in the financial year in which the obligation falls due". The effect of this rule is that it will no longer be possible to refer "legal obligations that did not fall due in the year" to the current financial year[33]. The provision therefore requires for the whole amount of the appropriated

33 *Corrado (2016).*

and committed sums, regardless of their financial manifestation, to be entered in the budget for the year in which the commitment is perfected. This provision, which calls for a precise orientation on the accounting of current expenditure, should allow greater control over expenditure and the effects on public finance balances for decentralised entities and central government. However, the problem remains as to how investment expenditure is to be properly accounted for and recognised in the budget. The tenor of the legislation **would appear to confirm that investment expenditure is not to be recorded in the financial year in which the financial coverage is identified, rather it should follow the gradually accruing state of progress rule, which is typical of investment expenditure**. The aim of the rule appears to be clear: it aims to minimise the formation of residual liabilities and make the public budget more transparent. The crucial point for Advanced Therapy Medicinal Products is, therefore, whether they can be considered investment expenditure, which produces long-term benefits, and therefore consequently, how this expenditure can be properly evaluated and accounted for. It could be argued that the majority of medical products, medicinal products and treatments can theoretically have the characteristics of investment expenditure. An anticoagulant (even common aspirin) or a medicinal product for blood pressure undeniably have long-term systemic effects on patient health, and therefore they could, theoretically, have the characteristics of an investment. Nevertheless, it is quite clear that there are medical protocols and specific advanced therapies (from vaccines to ATMPs) for which the investment element is far more obvious and indisputable. In the case of a medicinal product for blood pressure, the long-term effect is produced after consistent and extended long-term use; and therefore the systemic effect on health is produced with the contribution of many other medical, social, dietary and environmental factors that are difficult to distinguish and isolate. Lastly, the cost of these medicinal products is decidedly low, they are characterised by a low price and with the de facto irrelevance of the dimensions of research and development and a completely different target group of treatable patients. Therefore, even if their systemic effects are recognised, they only have a small investment component and they are akin to the consumption of a common medicinal product.

Appendix C
Consumption expenditure

Final consumption expenditure (from ESA 2010)

Final consumption expenditure is expenditure on goods and services used by households, NPISHs and government to satisfy individual and collective needs. In contrast, actual final consumption refers to its acquisition of consumption goods and services. The difference between these concepts lies in the treatment of certain goods and services financed by the government or NPISHs but supplied to households as social transfers in kind.

Final consumption expenditure (P.3)

3.94 *Definition:* final consumption expenditure consists of expenditure incurred by resident institutional units on goods or services that are used for the direct satisfaction of individual needs or wants or the collective needs of members of the community.

3.95 Household final consumption expenditure includes the following examples:
(d) items not treated as capital formation, in particular consumer durables, that continue to perform their function in several accounting periods; this includes the transfer of ownership of some durables from an enterprise to a household.

Actual final consumption (P.4)

3.100 *Definition*: actual final consumption consists of the goods or services that are acquired by resident institutional units for the direct satisfaction of human needs, whether individual or collective.

3.101 *Definition*: goods and services for individual consumption ('individual goods and services') are goods and services acquired by a household and used to satisfy the needs and wants of members of that household. Individual goods and services have the following characteristics:

- it is possible to observe and record the acquisition of the goods and services by an individual household or member thereof and also the time at which the acquisition took place;
- the household has agreed to the provision of the goods and services and takes the action necessary to consume the goods and services, for example by attending a school or clinic;
- the goods and services are such that their acquisition by one household or person, or by a group of persons, precludes its acquisition by other households or persons.

3.102 *Definition*: collective services are services for collective consumption that are provided simultaneously to all members of the community or all members of a particular section of the community, such as all households living in a particular region. Collective services have the following characteristics:

- they can be delivered simultaneously to every member of the community or to particular sections of the community, such as those in a particular region or locality;
- the use of such services is usually passive and does not require the agreement or active participation of all the individuals concerned;
- the provision of a collective service to one individual does not reduce the amount available to other in the same community or section of the community.

3.103 All household final consumption expenditure is individual. All goods and services provided by NPISHs are treated as individual.

3.104 For the goods and services provided by government units, the borderline between individual and collective goods and services is drawn on the basis of the classification of the functions of government (COFOG).

All government final consumption expenditure under each of the following headings is treated as expenditure on individual consumption:

- 7.1 Medical products, appliances and equipment;

- 7.2 Outpatient services;
- 7.3 Hospital services;
- 7.4 Public health services.

3.105 Alternatively individual consumption expenditure of general government corresponds to division 14 of the classification of individual consumption by purpose (Coicop), which includes the following groups:

- 14.2 Health (equivalent to COFOG groups 7.1 to 7.4).

3.106 Collective consumption expenditure is the remainder of the government final consumption expenditure.

- It consists of the following COFOG groups:
- general public services (division 1);
- defence (division 2);
- public order and safety (division 3);
- economic affairs (division 4);
- environmental protection (division 5);
- housing and community amenities (division 6);
- general administration, regulation, dissemination of general information and statistics (all divisions);
- research and development (all divisions).

Consumer durables

Consumer durables are coded using X as a prefix plus DHHCE (durable household consumption expenditure) plus a one-digit affix for subgroups and two digits for the items. The corresponding Coicop numbers are also provided.

Coicop	SNA codes	
XDHHCE1		Furniture and household appliances
05.1.1	XDHHCE11	Furniture and furnishings
05.1.2	XDHHCE12	Carpets and other floor coverings
05.3.1	XDHHCE13	Major household appliances whether electric or not
05.5.1	XDHHCE14	Major tools and equipment for house and garden
XDHHCE2		Personal transport equipment
07.1.1	XDHHCE21	Motor cars
07.1.2	XDHHCE22	Motor cycles
07.1.3	XDHHCE23	Bicycles
07.1.4	XDHHCE24	Animal drawn vehicles
XDHHCE3		Recreational and entertainment goods
08.2.0	XDHHCE31	Telephone and telefax equipment
09.1.1	XDHHCE32	Equipment for the reception, recording and reproduction of sound and pictures
09.1.2	XDHHCE33	Photographic and cinematographic equipment and optical instruments
09.1.3	XDHHCE34	Information processing equipment
09.2.1	XDHHCE35	Major durables for outdoor recreation
09.2.2	XDHHCE36	Musical instruments and major durables for indoor recreation
XDHHCE4		Other durable goods
12.3.1	XDHHCE41	Jewellery, clocks and watches
06.1.3	XDHHCE42	Therapeutic medical appliances and equipment

Goods being withdrawn are valued at the time of withdrawal.

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