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Subject:	COMMISSION STAFF WORKING DOCUMENT EVALUATION of the Regulation (EC) No 469/2009 of the European Parliament and of the Council concerning the supplementary protection certificate for medicinal products, and Regulation (EC) No 1610/96 of the European Parliament and of the Council concerning the creation of a supplementary protection certificate for plant protection products.

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COMMISSION STAFF WORKING DOCUMENT

EVALUATION

of the

Regulation (EC) No 469/2009 of the European Parliament and of the Council concerning the supplementary protection certificate for medicinal products, and Regulation (EC) No 1610/96 of the European Parliament and of the Council concerning the creation of a supplementary protection certificate for plant protection products.

{SWD(2020) 293 final}

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Glossary

Term/Acronym	Meaning/Definition
Accessibility	The extent to which a medicine is authorised, marketed and reimbursed in an EU Member State, and therefore may be actually used by a patient.
Affordability	The extent to which patients are able to make out-of-pocket payments on health care, or able to make co-payments in some form (affordability at micro level), and the extent to which public funding of the health care sector raised through premia or taxes is sustainable (affordability at macro level).
Availability	The extent to which a medicine exists (to treat a certain condition) and has been authorised (in an EU Member State or centrally in the EU), without necessarily being marketed.
API	Active pharmaceutical ingredient. This is the component of a medicine or plant protection product (e.g. a pesticide) that produces its effects.
Biopharmaceuticals or biologics	A medicine whose active substance is made by a living organism. Biological medicines contain active substances from a biological source, such as living cells or organisms (from humans, animals and microorganisms such as bacteria or yeast). The European Medicine Agency (EMA) evaluates biologics in the EU.
Biosimilar medicine or biosimilar	A biosimilar is a biological medicine highly similar to another already approved biological medicine. Biosimilars are approved according to the same standards of pharmaceutical quality, safety and efficacy that apply to all biological medicines.
Biotechnology (short: biotech)	Technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for a specific use.
Bolar exemption	The Bolar exemption makes it possible to conduct the testing required to obtain regulatory approval for the generic/biosimilar to take place during the patent/supplementary-protection-certificate (SPC) protection period of the reference medicine. The rationale for this exemption is to allow for the swift introduction of generic medicines shortly after the expiry of the patent/SPC term of the original product. Otherwise, in the absence of a Bolar exemption, tests for regulatory approval of generic medicines could only be conducted after patent/SPC expiry of the reference medicine, which would delay their market entry by months or even years. The EU Bolar exemption is laid down in Article 10(6) of Directive 2001/83/EC and Article 41 of Regulation (EU) 2019/6 (formerly Article 13(6) of Directive 2001/82/EC).
Data protection (See entry below on 'market protection')	Period of protection (of 8 years) during which pre-clinical and clinical data and data from clinical trials handed in to the authorities by one company cannot be referenced by another company in their regulatory filings.
EMA	European Medicines Agency
Effective protection period	The period that elapses from the time a product obtains a marketing authorisation until the last measure of protection (e.g. SPC, market protection, patents) on it expires.
FDA	US Food and Drug Administration

Generic medicines (‘generics’)	A generic medicinal product is a copy of an original non-biologic ‘reference medicinal product’ whose intellectual property rights (IPR) and market protection has lapsed or expired. The generic medicine is usually manufactured by a different company. Generics have the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal products.
Manufacturer of generics and biosimilars	This term includes manufacturers of generics and/or biosimilars as well as manufacturers of APIs corresponding to those generics/biosimilars.
Marketing Authorisation (MA)	The approval to market a medicine in one, several or all Member States.
Marketing Authorisation application	An application made to a European regulatory authority for approval to market a medicine within the European Union.
Market protection	The period of protection during which generics, or biosimilars, cannot be placed on the market (typically 10 years from the marketing authorisation).
Originators or innovators	The companies which develop new medicines or active ingredients. They are typically the SPC holders, but are increasingly becoming leaders in the production and commercialisation of biosimilars.
Paediatric rewards and Paediatric Regulation (**)	The Paediatric Regulation (**) has governed the development and authorisation of medicines for paediatric use since entering into force in 2007. Its objective is to improve the health of children in Europe by addressing the low level of research and development in medicines for children. The Regulation sets up a system of obligations, rewards and incentives to encourage clinical research and development in medicines for children. (**) Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (Text with EEA relevance)
Personalised medicine	A medical treatment using analysis of individuals’ phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) to: (i) tailor the right therapeutic strategy for the right person at the right time; (ii) determine a person’s predisposition to disease; or (iii) deliver timely and targeted prevention.
PPP	Plant protection product (e.g. a pesticide).
R&D / R&I	Research and development / Research and innovation
SPC	A supplementary protection certificate is a *sui generis* intellectual property right that extends by up to 5 years the effect of a patent in a Member State (with an extra 6 months possibly added for SPCs for medicinal products, if a paediatric investigation plan is conducted). SPCs apply to human medicinal produts, or to plant protection products, subject to regulatory authorisation.
SPC manufacturing waiver	An exception to the rights conferred by SPCs for medicinal products, as set out by Regulation (EU) 2019/933. This exception allows – under specific conditions: (i) the manufacturing of a product protected by an SPC in order to export the product outside the EU; or (ii) the storing of a product protected by an SPC before placing it on the EU market after SPC expiry.
TRIPS	Agreement of the World Trade Organization (WTO) on Trade-Related Aspects of Intellectual Property Rights.

Unitary patent (NOTE: Unitary patents were not yet in force at the date of publication of this staff working document)	Term used to describe a 'European patent with unitary effect' laid down by Regulations No 1257/2012 and 1260/2012, which is a European patent granted under the European Patent Convention, to which unitary effect is attributed at the request of its proprietor. The unitary effect will cover all Member States (MS) participating in the enhanced cooperation for unitary patent protection and which have ratified the Unified Patent Court ('UPC') Agreement, in accordance with which litigation relating to European (including unitary) patents and related SPCs will take place. As of September 2020, the unitary patent system (including the UPC) is not yet operational.
Unmet medical need	A condition for which there exists no satisfactory method of diagnosis, prevention or treatment, or if such a method exists, it should bring major therapeutic advantage to those affected (see Art. 4 (2) of Regulation (EC) No. 507/2006). However, there is so far no agreement on the definition of unmet medical need among patients, industry players, regulators, health-technology assessment bodies, and payers. The concept may include a lack of access to existing products[1].

[1] https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Unmet_health_care_needs_statistics#General_overview

1 INTRODUCTION

The present Commission staff working document provides an ex-post evaluation of Regulation (EC) No 469/2009 of the European Parliament and of the Council (codified version) and Regulation (EC) No 1610/96 of the European Parliament and of the Council, on supplementary protection certificates (SPCs) for medicinal products (pharmaceuticals) and plant protection products (PPPs, e.g. pesticides) respectively (hereafter mostly referred in the text as "SPC Regulations"). The evaluation assesses whether the main objectives of these two SPC Regulations (see Section 2.2 below) have been achieved. The following criteria are taken into account by the evaluation: effectiveness, efficiency, relevance and added value of the EU intervention. The evaluation also reviews both the internal coherence of the SPC Regulations and their external coherence with: (i) the regulatory incentives enshrined in EU pharmaceutical legislation (including orphan incentives and paediatric rewards); (ii) the applicable patent framework in the EU; and (iii) the EU's international commitments.

The Health Council conclusions of June 2016[2] called upon the Commission to engage in a wider review of incentives in the pharmaceutical sector. The Council invited the Commission to conduct an evidence-based analysis of the impact of EU pharmaceutical incentives on the innovation, availability and accessibility of medicinal products. Among those incentives, the Council considered that particular attention should be given to SPCs for medicinal products and the Bolar exemption (which applies to pharmaceutical patents and SPCs).

The Commission published an inception impact assessment in February 2017, announcing a back-to-back evaluation and impact assessment of all relevant provisions and options for modernising the SPC Regulations. In October 2017, the Commission launched a 12-week online public consultation[3] (see Annex 2). Several studies on SPC protection have been contracted or conducted within the European Commission since 2015 (see Section 4.1 below).

The SPC for medicinal products is an incentive for pharmaceutical research, which plays a decisive role in the continuing improvement of public health[4]. In view of Council conclusions mentioned above, this evaluation includes and assessment of the impact of the SPC on the availability (e.g. supply shortages[5] and deferred or missed market launches of innovative

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[2] Paragraph 47 of the Council Conclusions on strengthening balance in the pharmaceutical systems in the EU and its Member States (17.6.2016) ask the Commission to:

Prepare as soon as possible and with the close involvement of the Member States, while fully respecting Member States competences, the following: an evidence based analysis of the impact of the incentives in these EU legislative instruments, as implemented, on innovation, as well as on the availability, inter alia supply shortages and deferred or missed market launches, and accessibility of medicinal products, including high priced essential medicinal products for conditions that pose a high burden for patients and health systems as well as availability of generic medicinal products. Among those incentives, particular attention should be given to the purpose of supplementary protection certificates as defined in the relevant EU legislative instrument and the use of the "Bolar" patent exemption, the data exclusivity for medicinal products and the market exclusivity for orphan medicinal products.

[3] That consultation included questions relating to procedural and substantive aspects of the SPC regulations, including a possible SPC manufacturing. These categories of questions were already asked as part of discussions about further future potential initiatives to modernise the SPC regime.

[4] Recital 2 of Regulation (EC) No 469/2009 states that 'pharmaceutical research plays a decisive role in the continuing improvement in public health'.

[5] See European Parliament resolution on the shortage of medicines – how to address an emerging problem - 2020/2071(INI)

medicines) and accessibility (e.g. launch of generic medicinal products and biosimilars) of medicinal products in the EU.

This is the first evaluation of the SPC Regulations. It covers the period from 1992 to October 2020 and considers all EU Member States during that period. It also takes into account recent case-law from the Court of Justice of the European Union (CJEU) and changes in the pharmaceutical and agrochemical sectors of the EU's main trading partners (see Section 5.1.2 for details).

This evaluation does not assess the narrow exemption ('SPC manufacturing waiver') introduced by Regulation (EU) 933/2019 of the European Parliament and of the Council, that is too recent to measure any impact and will be the subject of specific future evaluations.

This evaluation takes place as part of the *IP action plan*[6] and of the *pharmaceutical strategy for Europe*[7]. It goes alongside the evaluation of the legislation on medicines for children and rare diseases.

2 BACKGROUND OF THE INTERVENTION

2.1 Description of the SPC system

An SPC is a sui generis intellectual property right that can extend by up to five years the protection conferred by a patent ("the basic patent"), but only with respect to the medicinal product, or plant protection product (PPP), that is covered by the related marketing authorisation. SPC protection for medicinal products was first introduced in the EU in 1992 through Council Regulation (EEC) No 1768/92 and is currently governed by Regulation (EC) No 469/2009 of the European Parliament and of the Council (codified version). In 1996, SPC protection for PPPs was established by Regulation (EC) No 1610/96 of the European Parliament and of the Council.

SPC protection aims at offsetting the loss of effective patent protection due to the length of the necessary testing, clinical/field trials and marketing authorisation procedures, thereby providing the pharmaceutical and PPP industries with incentives to innovate.

As shown in Figure 1 below, an SPC takes effect at the end of the term of the basic patent, and is granted for a period equal to the period which elapsed between the date on which the application for a basic patent was filed and the date of the grant of the first authorisation to place the patented product on the market in the EU, reduced by five years, and with a maximum duration of five years. Some patented products may thus not be eligible for SPC protection at all, i.e. if the marketing authorisation was obtained in less than 5 years after the filing of the application for the basic patent; some may enjoy SPC protection having the full duration of 5 years; while others enjoy SPC protection of a shorter duration. The average duration of SPCs for medicinal products granted in the EU amounts to 3.5 years[8].

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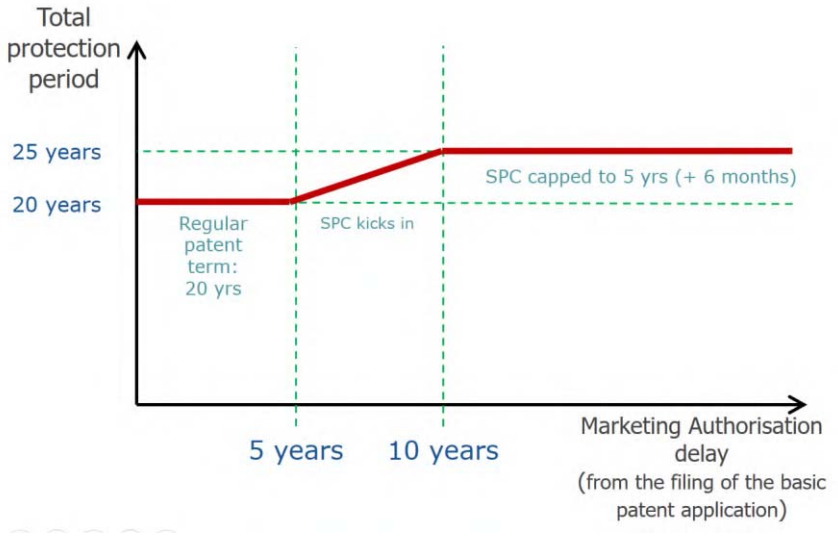
6 https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12510-Intellectual-Property-Action-Plan

7 https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12421-Pharmaceutical-Strategy-Timely-patient-access-to-affordable-medicines

8 Source: Copenhagen Economics study of 2018 (see Section 4 and annex 3).

Figure 1: Duration of the SPC



Following the request of the holder of an SPC for medicinal products, the duration of the SPC can be extended once by six months in the case where Article 36 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use applies (namely that all the measures included in an agreed paediatric investigation plan are complied with, the protected product is authorised in all Member States and relevant information on the results of studies is included in product information).

Since an SPC '*confer[s] the same rights as conferred by the basic patent*' (Articles 5 of the SPC Regulations), the exclusivity resulting from the basic patent is extended and enables its holder to prevent competitors from practicing the invention (e.g. manufacturing, offering for sale or storing generic products) in those Member States in which an SPC has been granted.

Some exemptions to the SPC rights for medicinal products apply, such as the Bolar exemption and the SPC manufacturing waiver. The Bolar exemption allows generics to be manufactured during the patent and SPC term for clinical trials purposes. The SPC manufacturing waiver allows, under certain conditions, generics to be manufactured during the SPC term for export or storing purposes.

As analysed in Section 5.1.3, the existing SPC system requires the filing of an SPC application in each of the EU Member States where SPC protection is sought. Each of the Member States concerned has to examine and publish the application and eventually grant or refuse the SPC. These nationally granted SPCs are enforced in national courts. In the absence of a unitary SPC title, this situation will remain the case even with the future introduction of the unitary patent system, with the exception that the currently nationally granted SPC might be centrally enforced before the future Unified Patent Court ('UPC') for the participating Member States (having ratified the UPC Agreement).

Section 3 below provides statistics on the use of the SPC in the EU.

Further to patents and SPCs, EU legislation provides pharmaceutical innovators with additional types of incentives and rewards such as data exclusivity and market protection (see glossary), orphan incentives and paediatric rewards. Annex 10 provides for graphics (source Copenhagen Economics (CE) study) on the related legislation (and its chronological introduction), duration and interaction of the EU constellation of incentives and rewards for

human medicinal products. Veterinary medicinal products can enjoy periods of protection of the technical documentation on quality, safety and efficacy originally submitted with a view to obtaining a marketing authorisation[9]. Innovators in the field of PPPs can also enjoy periods of regulatory data protection or exclusive use to safety and efficacy data in the registration dossier necessary for marketing authorisation of chemical plant protection products[10].

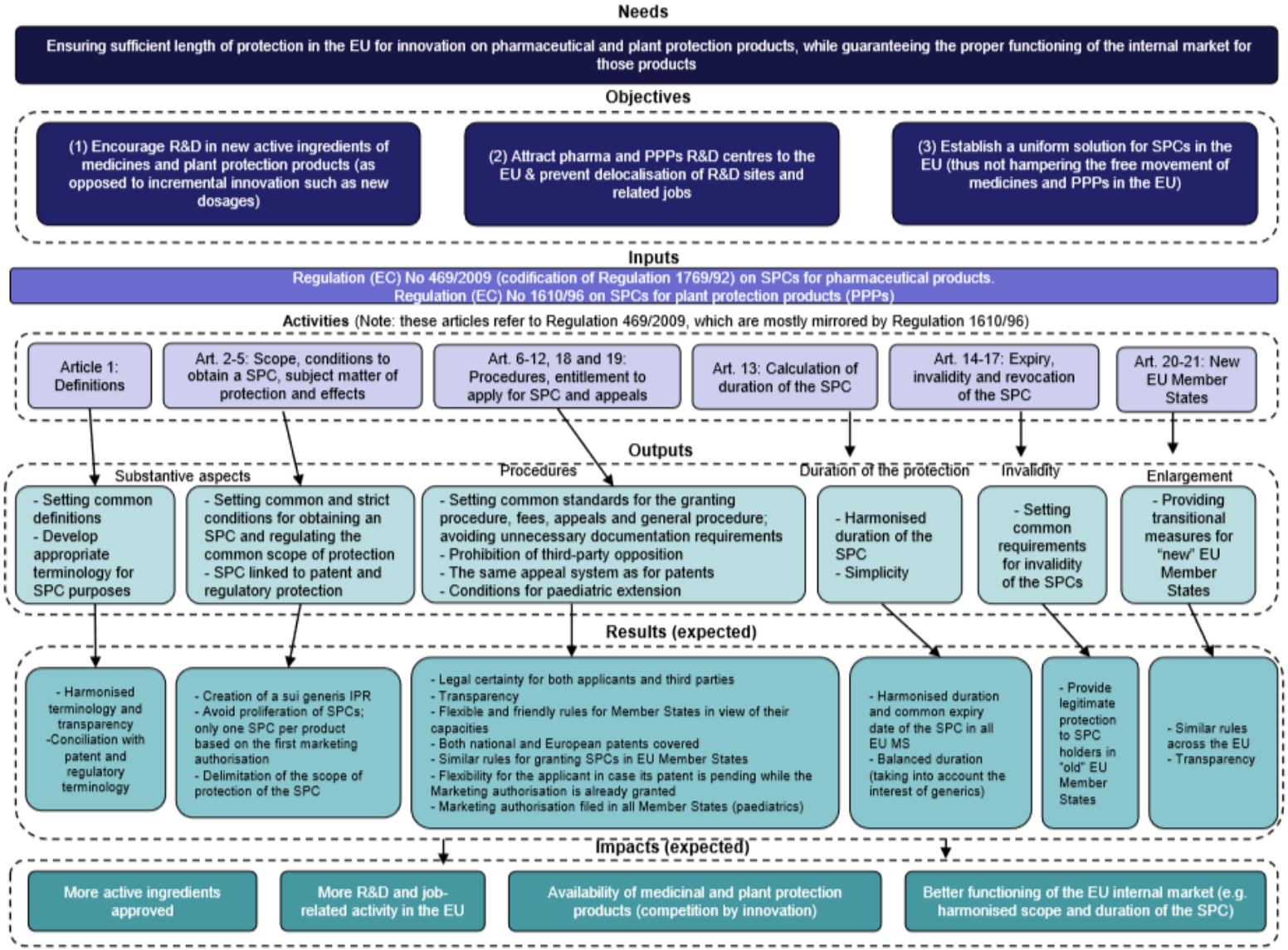
2.2 Description of the intervention logic and objectives of the SPC

The following graphic depicts the intervention logic for the EU SPC legislation when the SPC system was established, including the objectives sought by the SPC protection.

[9] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC.

[10] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.

Evaluation of EU legislation on supplementary protection certificates (SPCs) – Intervention logic



The first objective of the SPC system is to encourage R&D in new active ingredients of medicines and PPPs at worldwide level (i.e. the location of the R&D is not relevant[11]) so that it could result in more availability of those products for EU patients and consumers of PPPs. External factors such as incentives and rewards in the EU pharmaceutical and PPPs legislations can contribute to additional investments and jobs in innovation and therefore to the availability of more active ingredients.

The second objective is about attracting R&D centres and jobs to the EU and preventing R&D delocalisation outside the EU, which was especially relevant in the 1990s considering the 'competition' of certain third countries that had introduced SPC-like legislation (e.g. 'patent term extensions').

The third objective is about promoting a homogenous SPC system in the EU. This would in particular prevent the heterogeneous development of national laws that would hamper the free movement of medicinal products and PPPs within the internal market.

The 2017 inception impact assessment for optimising the Internal Market's industrial property legal framework relating to supplementary protection certificates (SPC)[12] identified unintended results that the SPC legislation brought for the EU-based manufacturers of generic and biosimilar medicines, namely the loss of export markets (third countries) and of day-1 entry onto EU Member State markets. The lawmakers had not anticipated in 1992 this negative impact of the SPC on the competitiveness of EU-based generics/biosimilars manufacturers. The impact assessment related to Regulation (EU) 2019/933[13] on the SPC manufacturing waiver analyses in detail those unintended results.

2.3 Mapping of relevant stakeholders

The following stakeholders have been consulted by the Commission through an online general public consultation (see Annex 2):

- Group I: General public, which can be users of medicines and PPPs.
- Group II: Innovative companies or originators, which apply for and enforce SPC protection. Originators are typically universities, start-ups, SMEs and large companies conducting research to develop new products (as opposed to generics manufacturers below).
- Group III: Companies dealing with generic medicines and generic PPPs, including producers of active pharmaceutical ingredients (APIs). They need to know the status and scope of SPCs across the EU to conduct their businesses. They can make use of flexibilities such as the Bolar exemption and the SPC manufacturing waiver.

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11 In this respect, the Technopolis study (2018) states that '*whilst the SPC regulation clearly embodies an intent to promote pharmaceutical innovation in Europe, it does not contain any provisions to favour innovation originating from Europe over that from elsewhere. Rather, all pharmaceutical innovation is treated equally, regardless of the country where the applicant is based or where the R&D has been performed. Consequently, the greatest economic returns from the SPC regulation appear destined to flow towards where the greatest research and innovation intensity is*.'

12 https://ec.europa.eu/smart-regulation/roadmaps/docs/2017_grow_051_supplementary_protection_certificates_en.pdf

13 https://ec.europa.eu/docsroom/documents/29463

- Group IV: EU large consumers/purchasers of PPPs or medicines; health professionals and associations; health or price-setting authorities, including ministries of health; and patients associations, which are interested in the availability and accessibility of innovative products.
- Group V: National authorities such as the IP offices and courts of EU Member States, which respectively grant and enforce SPCs; IP agents and attorneys who deal with the registration, monitoring and enforcement of SPCs.
- Group VI: industry/trade authorities, which monitor and manage incentives for industrial investments and trade.

A total of 231 replies were provided to the Commission online consultation: 43 replies from the general public (Group I above), 71 from originators industry/associations (Group II), 63 from generics and biosimilars industry/associations (Group III), 15 from health authorities/doctors/patients groups (mostly from national organisations dealing with health insurance/reimbursement/health technology assessment, from a doctors' organisation, and 2 from patients' associations) (Group IV), 34 from patent offices/practitioners (Group V), and 5 from industry/trade authorities (Group VI).

In addition, the Max Planck Institute conducted a number of surveys among stakeholders in the Groups II, III and V above as part of the study on the legal aspects of the SPC contracted by the Commission (see Section 4.1).

2.4 Baseline and points of comparison

In the 1990s, the Commission did not conduct a formal impact assessment for the SPC Regulations as it was not yet part of the procedure for adopting a proposal until 2004. Therefore, the baseline has been reconstructed as far as possible based on available data, including by reference to the explanatory memorandum[14].

In Section 5, the analysis of the evolution of investments in innovation and job creation will be mostly benchmarked against the situation of the SPC system in the EU in 1992 (for medicines) and 1996 (for PPPs) when the SPC Regulations were adopted (the 'base scenario'). As of the adoption of those regulations, concerned patent holders had certainty that they could obtain SPC protection in the EU. In 1990, when the Commission proposed legislation on the SPC for medicinal products, the USA and Japan had, since 1984 and 1988 respectively, started providing patent term restoration for pharmaceutical roducts on their national markets also for a maximum period of 5 years.

In a counterfactual scenario, if the SPC Regulations had not been adopted at EU level, similar measures might have been introduced in most EU Member States through national legislation (in 1991, France and Italy had adopted national SPC legislations) likely in a non-uniform way.

[14] Explanatory Memorandum to the Proposal for a European Parliament and Council Regulation (EC), of 11 April 1990, concerning the creation of a supplementary protection certificate for medicinal products (COM(90) 101 final)

3 IMPLEMENTATION / STATE OF PLAY

The SPC Regulations have been implemented by all EU Member States (EU MS) (see Mejer study (2017)). No infringement actions against EU MS have been brought in relation to their implementation. In all EU MS, national IP offices have been entrusted with examining SPC applications and granting SPCs. National courts deal with their enforcement but also with appeals against refusals to grant or challenges to the validity of SPCs. National courts are also responsible for referrals to the CJEU on the interpretation of the SPC Regulations.

Since the entry into force of the SPC Regulations, the use of SPC protection has been steadily increasing. The average number of SPC applications in EU MS, combining both pharmaceutical and PPP SPCs, remained at the level of 30 applications annually between 1996 (year of adoption of the SPC Regulation on PPPs) and 2004, and then shifted to about 50 applications annually (see Mejer study (2017) for more details). The highest number of SPC filings has been recorded in the biggest markets (Germany, France, Italy and UK). Kyle study (2017) shows that the share of new medicinal products (i.e. active ingredients for the purpose of the SPC) obtaining an SPC in at least one Member State increased from 75% in the early 1990s to 86% to 2017. More than 20,000 SPC applications have been filed in the EU since the entry into force of the SPC Regulations.

Many more SPCs are applied and granted for medicinal products than for PPPs. For example, according to the Kyle study (2017), 197 plant protection SPC applications were lapsed, in force, or pending in 2015 in Germany, compared to 1,257 for medicinal products.

By 2016, more than 40 medicinal products had been granted an SPC extension by the national patent offices in one or more Member States, resulting in over 500 national extensions.

4 METHOD

4.1 Methodology and sources of information

A legal analysis of the SPC legislation has been conducted in-house and through several external studies, especially the Max Planck Institute study on the legal aspects of the SPC system (see Annex 3 on studies). This study analysed in detailed each of the provisions of the SPC Regulations, and was based on desk research and surveys to stakeholders (SPC holders and generics manufacturers and associations, IP attorneys, patent offices and judges), which were based on highly technical and detailed questionnaires. In the context of that study, two workshops with stakeholders were organised.

Economic analyses of the SPC system have also been conducted both in-house (e.g. Mejer study (2017)) and through external studies like the Copenhagen Economics study (see Annex 3 on studies), which analyses the economics of the SPC and other EU pharmaceutical incentives and how they interact. The latter also included several case studies.

The Commission conducted an online public consultation on the SPC system and the EU Bolar exemption from 12 October 2017 to 4 January 2018 (hereinafter Commission consultation). Its outcomes are summarised in document SWD(2018)242[15] (see Annex 2).

[15] https://ec.europa.eu/docsroom/documents/29464

4.2 Limitations and robustness of findings

In order to evaluate whether the first and second objectives identified in the intervention logic have been met, time-series data on R&D expenditures (at project level) and numbers of new chemical entities and new biologic entities launches in the EU are required for both the pharmaceutical and PPPs sectors. A main challenge in this evaluation is the collection of historical data in this regard as:

- The first SPC Regulation dates back to 1992, therefore the time-series data for the last three decades were needed. While R&D data is available and provided by public sources (OECD), there is no distinction between generic and innovator companies. The evaluation thus attributes all R&D to the innovative industry (this is not a major limitation as innovators invest considerably more on R&D than generics, even if the latter's R&D investment is far from being insignificant especially since the emergence of biosimilars and complex generics). Data on PPPs is scarce as confirmed by the CE (2018) and Kyle (2017) studies.
- Fragmentation of the EU framework prior to the establishment of the European Medicine Agency ('EMA') in 1995 makes it challenging to count the number of new chemical entities and new biologic entities launches in the EU. Prior to 1995, new chemical entities (NCEs) were approved at a national level. To have consistent long term series, Section 5.1.1 takes as a proxy[16] for the yearly generation of NCEs at world level the annual approvals of "novel drugs"[17] by the Center for Drug Evaluation and Research of the US Federal Drug Administration. Several studies are based on that data.[18] Section 5.1.1 also contrasts data from the US FDA with some recent data from EMA, and table 2 of the Kyle study of 2019, that confirm the trends are similar.

Finally, data on the R&D costs of development of individual, or groups of, medicines is not available, or partly available only via private database subscriptions.

A causality analysis between the introduction of the EU-level SPC legislation and the evolution of investments in R&D and registration of active ingredients in the pharmaceutical and PPPs sectors is further complicated by the fact that other external factors can have a significant impact on that evolution (see Section 5.1.1 for details). Indeed, quantifying the impact of intellectual property rights on innovation in any field of technology is a well-known challenge and the SPC framework is no exception in this respect. This limitation of the causality analysis is discussed in Kyle (2017), CE (2018) and Mejer (2017) studies.

Evaluating the first objective is particularly challenging as the levels of R&D spending in Europe are influenced by reforms of the regulatory framework related to pharmaceutical and

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[16] The use of this proxy can be found in several studies. See pages 203 and 219 of CE study.

[17] According to the annual reporting documentation of the Center for Drug Evaluation and Research of the US Federal Drug Administration (FDA), 'novel drugs' are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient treatments. The active ingredient or ingredients in a novel drug have never before been approved in the United States. These 'novel drugs' are approved either as new molecular entities (NMEs) under New Drug Applications (NDAs), or as new therapeutic biologics under Biologics License Applications (BLAs). In some cases, an NME may have actions similar to earlier drugs and may not necessarily offer unique clinical advantages over existing therapies (https://www.fda.gov/media/134493/download).

[18] C. F. Munos, B. (2009). Lessons from 60 years of pharmaceutical innovation. *Nature reviews Medicine discovery*, *8*(12), 959 and https://www.nature.com/articles/s41587-019-0021-6.

PPP products in both in the EU and USA. This is because, while R&D is local in a sense that R&D is undertaken in specific country, drug development efforts are global (i.e. R&D in one country, when successful, leads to sales in many countries).

Due to these limitations, this evaluation presents trends and correlations. Still, the analysis is robust as it draws on a number of different economic and legal studies (see Annex 3) whose results point to the same conclusions. Furthermore, in the analysis of SPC applications, the evaluation relies on high-quality (i.e. complete and detailed) data. That makes the evaluation results of the third objective particularly robust. Finally, trends and correlations found in the studies are in line with the feedback obtained from stakeholders in public consultations.

5 ANALYSIS AND ANSWERS TO THE EVALUATION QUESTIONS

The Commission's rules on *Better Regulation* outline five evaluation criteria: effectiveness, efficiency, relevance, coherence and EU added value.

For each of the five evaluation criteria and each of the three legislative objectives set out in the intervention logic of Section 2.2 (encouraging innovation, preventing delocalisation and providing uniformity), a set of evaluation questions (see Annex 8) was designed. This section analyses the SPC Regulations on the basis of those questions and provides answers.

The design of the questions took into account the elements of the intervention logic of Section 2.2 above and major policy developments related to the pharmaceutical and agrochemical sectors.

5.1 Effectiveness

The effectiveness analysis considers how successful the SPC Regulations have been in achieving their three objectives.

5.1.1 Objective 1: Encouraging global innovation in new products for EU patients and consumers of PPPs

The main aim of the SPC system is to promote the development of new active ingredients in the pharmaceutical and PPP sectors (not incremental innovation such as repurposing of known active ingredients for new treatments, new formulations, new dosages of existing medicines, or combining existing active ingredients with non-active ingredients).

As explained in the intervention logic, this first objective will be evaluated disregarding the geographical location of the R&D. It would be sufficient that the SPC contributes to worldwide research in new active ingredients as long as EU patients and farmers can benefit from that global research (induced by EU and non-EU countries) through the availability of more products (i.e. more registration of active pharmaceutical and PPP ingredients in the EU). Conversely, the second objective (attracting R&D to the EU and preventing R&D delocalisation outside the EU), analysed in Section 5.1.2, has a geographical focus on the EU.

- Question 1: Has worldwide innovation in new active ingredients increased since the introduction of the SPC system?

Pharmaceutical sector

The pharmaceutical industry remains a leading industrial sector in R&D investment. Figure 2 below shows the development since 1975 of business expenditure on R&D for the pharmaceutical industry in the US, Japan, Canada, Australia and 10 EU Member States[19]. Figure 2 also shows, as a benchmark, the development of R&D expenditure in the whole manufacturing sector. The two vertical dotted lines indicate the dates on which SPC systems were introduced in the USA (in 1984) and in the EU (in 1992).

Figure 2: Development of R&D investment in the pharmaceutical industry and manufacturing industry in general (Source: OECD ANBERD database)

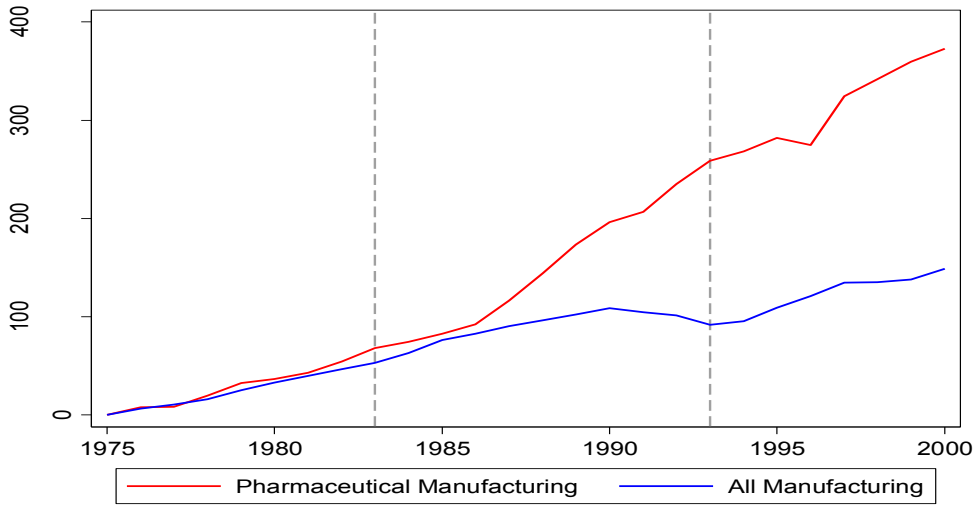

Figure 2 shows that the pharmaceutical industry has devoted significantly more resources to R&D investment since the mid-1980s than the aggregated manufacturing sector. Moreover, unlike other industries, the pharmaceutical industry continued to accelerate its investment in R&D in the first half of the 1990s.

However, not all this worldwide pharmaceutical investment in R&D is necessarily devoted to the development of new active ingredients, the subject-matter of SPC protection. For example, a part of this R&D investment may be devoted to finding additional therapeutic uses for existing active ingredients. Therefore, to further ascertain the effectiveness of this first objective, the evaluation analysed the evolution of approvals of new active ingredients (this also helps in analysing the efficiency of the SPC).

As discussed in Section 4.2 above, the evaluation takes the annual approvals of 'novel drugs' by the Center for Drug Evaluation and Research of the US FDA as a proxy[20] for the generation of 'new active ingredients' at world level. It can be observed that the increasing

[19] Belgium, Denmark, Finland, France, Germany, Italy, the Netherlands, Spain, Sweden and the UK.

[20] The use of this proxy can be found in several studies. See pages 203 and 219 of the CE study.

investment in R&D was accompanied by more approvals of new active ingredients over several decades as observed in Figure 3 and Figure 4[21,22], especially during the last decade (see detailed analysis in Annex 5). However, there was a decline in approvals of novel medicines in the first decade of the 2000s following the approvals spiked in the late 90s in the context of the Prescription Drug User Fee Act (PDUFA) of 1992[23]. PDUFA introduced measures for the FDA to eliminate the backlog of un-reviewed applications within 24 months of the establishment of an user fee program.

An OECD[24] study and many others discuss that the efficiency of pharmaceutical R&D has been declining (Eroom's law in pharmaceutical R&D) in recent decades (with a stable trend in the past decade) due to several interrelated factors. The OECD study explains that this phenomenon can also be found in other sectors, including the PPP sector, and implies that ideas/treatments that are 'easy' to find are developed and exploited first. Then, as the stock of knowledge increases, new ideas/treatments become harder to find or inventions and output can only be sustained or increased by large increases in research effort that offset declining productivity. In pharmaceuticals, this is apparent in an ever-increasing back catalogue of effective drugs, and a shift towards more complex conditions that has increased the complexity of clinical trials and failure rates[25]. Another hypothesis is that more stringent requirements to gain marketing authorisation have also increased the costs of clinical trials. On the other hand, declines in productivity are also driven by rising R&D costs.

A similar patterm of the historical approvals of novel drugs observed in the US FDA data in recent decades can be also observed in data for approvals of new human and veterinary active

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21 Munos B. (2009), Lessons from 60 years of pharmaceutical innovation. *Nature Reviews Drug Discovery*, *8*(12), 959.

22 https://www.nature.com/articles/s41587-019-0021-6

23 Mary K. Olson, PDUFA and Initial U.S. Drug Launches, 15 Mich. Telecomm. Tech. L. Rev. 393 (2009)

24 OECD study 'Pharmaceutical Innovation and Access to Medicines' (2018).

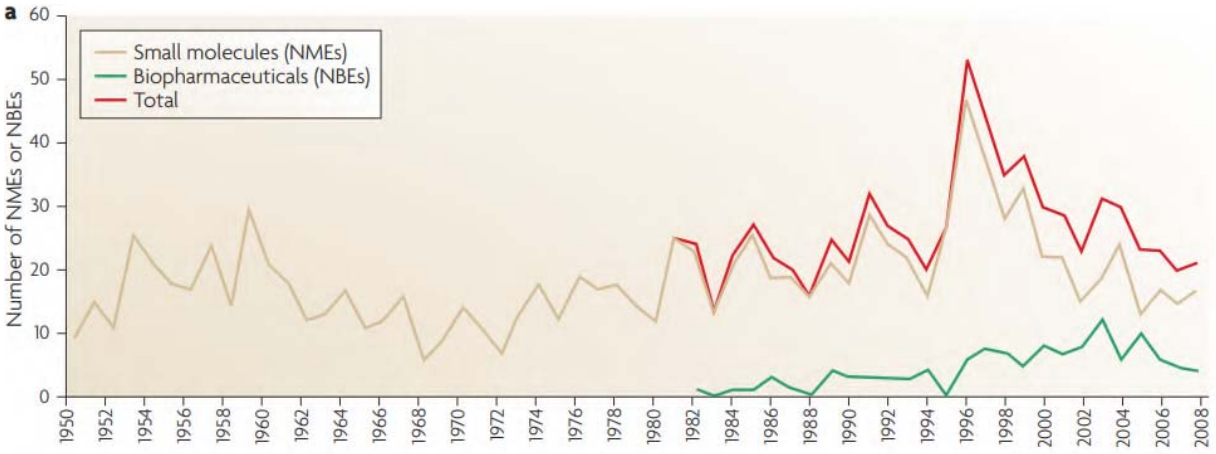
25 Scannell et al., 2012; Deloitte Centre for Health Solutions, 2016; SSR Health, 2016.

substances at the European Medicines Agency (see

Figure 5), and in the evolution observed by the Kyle study of 2019 for the period between 1990 and 2015 at global level (see Figure 6).

Specifically for biologicals[26], the figures below show a positive trend in the generation of new active ingredients since the emergence of biotechnology in the 1980s.

Figure 3: US FDA approvals of new molecular entities (NMEs)[27] from 1950 to 2008



[26] As discussed under Section 5.3 (relevance) biologics are eligible for SPC protection.

[27] New Molecular Entity, i.e. an active ingredient that contains no active moiety that has been previously approved by the FDA or has been previously marketed as a drug in the USA.

Figure 4: US FDA approvals of new molecular entities (NMEs) from 1998 to 2018
(Source: FDA databases)

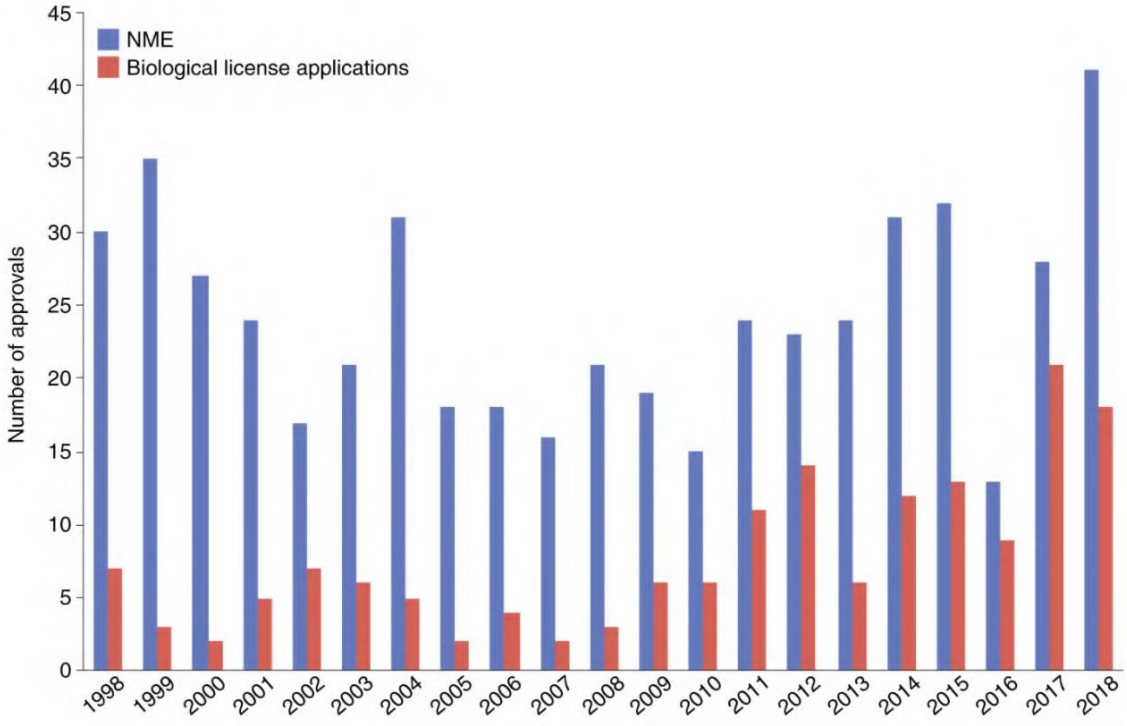
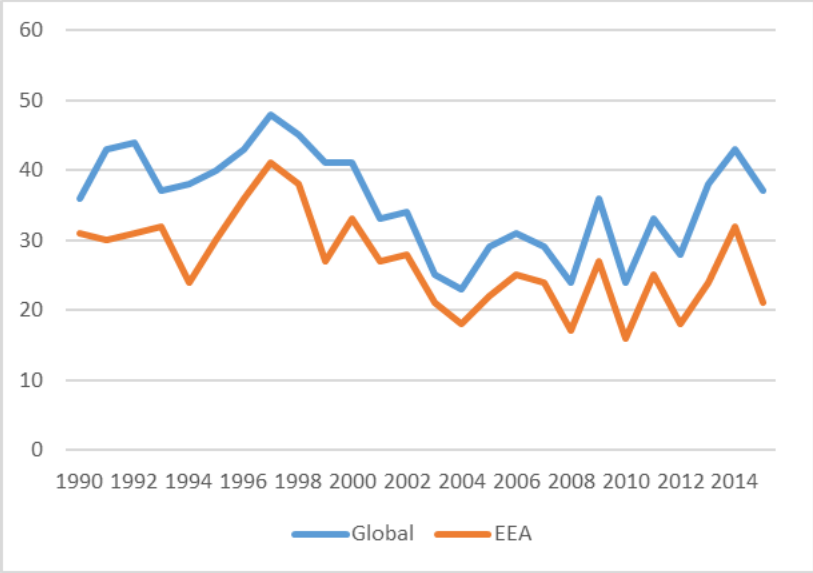


Figure 5: Number of annual EU centrally authorised human and veterinary products for new active substances (Source: data provided by EMA)

Figure 6: New chemical entitites launched annually - both globally and in the European Economic Area (EEA) (Source: data from Table 2 of Kyle study of 2019)



PPP sector

A specialised study by consultants Phillips McDougall in 2013[28] reported that annual industry expenditure on crop protection R&D worldwide more than doubled from USD 3.06 billion to USD 6.71 billion between 1995 and 2012. A Phillips McDougall survey in 2016 of 11 companies reported annual, total, agrochemical-industry-R&D expenditure of USD 2.6 billion in 2014 and USD 3.2 billion in 2019.

A subsequent 2019 study by Phillips McDougall AgriService[29] highlights that investment in R&D in PPPs remains high compared to other industrial sectors. Major companies (many of them EU-headquartered) invested around 10% of their annual sales in R&D over the last 50 years. The study also states that the total number of active PPP ingredients available globally has been increasing for decades, from 400 at the beginning of the 1990s to 600 at the beginning of the 2010s[30].

However, unlike in the pharmaceutical sector, the annual number of new active ingredients introduced for conventional crop protection has declined in recent decades in global markets according to Phillips McDougell database and analysis (Figure 7). According to a study by Deloitte[31], this global decline is due to two main factors, set out in the bullet points below.

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28 R&D trends for chemical crop protection products and the position of the European Market, Phillips McDougall for ECPA, September 2013.

29 Evolution of the Crop Protection Industry since 1960, Phillips McDougall, November 2018.

30 In 1960, there were 15 chemical classes on the market, whereas today's products come from more than 40 different classes. New chemical classes often bring with them new modes of action which are important for addressing problems of resistance, whether to insecticides, fungicides or herbicides.

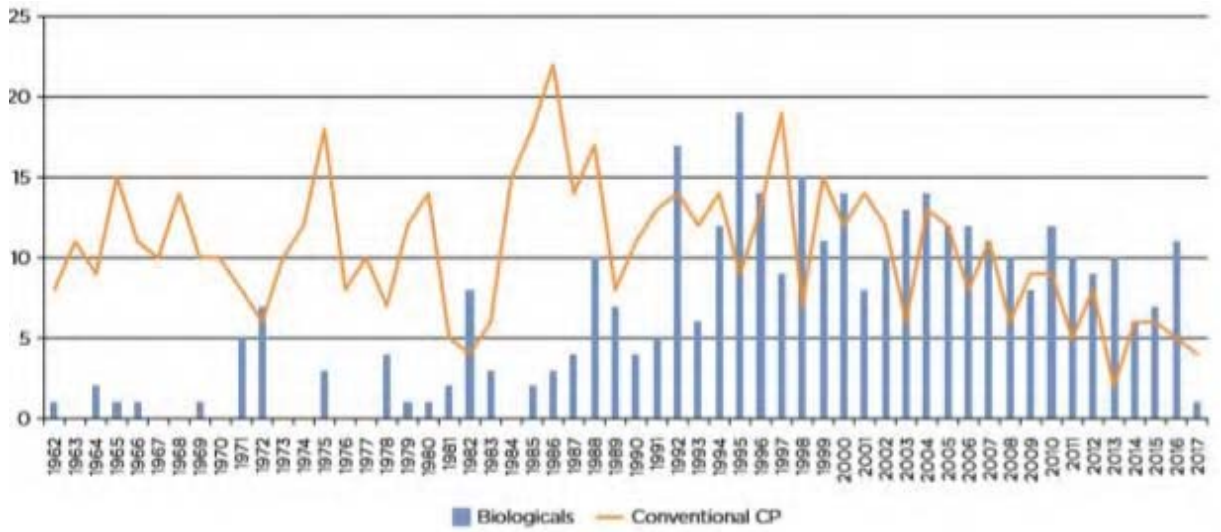
31 Deloitte's report on the future of agrochemicals (2019) https://www2.deloitte.com/content/dam/Deloitte/us/Documents/energy-resources/us-eri-future-of-agrochemicals.pdf. This report describes other discouraging factors, such as a reduction in government farm subsidies and the accelerated pace of change in farming markets (the long-term demand for PPPs could be

- Longer product-development cycles and escalating costs: the average development period for a new PPP has increased from 8.3 years in 1995 to 11.3 years in 2010-2014. This has increased the overall R&D costs for a new PPP from USD 152 million in 1995 to USD 286 million in 2010-2014.
- Increasing stringency of regulatory requirements: this hampers the further development of innovative technologies and the use of some types of crop-protection agents like glyphosate.

This global trend of decreasing numbers of new active ingredients can also be observed at EU level. The 2013 study by Phillips McDougall points to a decline in investment in R&D for new PPPs that is specific to the European market (with fewer new active substances being registered in the EU). They conclude that there are three possible reasons for this: (i) the maturity of demand in the EU (compared with other world regions like Asia); (ii) increasingly stringent data requirements for regulation; and (iii) the non-acceptance of genetically modified seeds in the EU. The study concludes that this leaves European farmers with fewer new technologies to drive agricultural production than their competitors in other regions of the world.

According to the 2013 study by Phillips McDougall, the number of companies worldwide involved in R&D of new active ingredients for PPPs has halved, from 35 companies in 1995 to 18 in 2012. This has arguably affected competition in new product areas[32].

Figure 7: Annual new PPP introductions for biologicals and conventional crop products worldwide (Source: Phillips McDougall)



reduced by: the use of advanced robotics, drones, artificial intelligence, gene editing, reduced biofuel demand, alternative meats, improved animal digestion, and indoor farming). This industrial sector has also shifted overall R&D expenditure toward seeds and traits.

[32] Between 2007 and 2012, the total agrochemical R&D expenditure of major companies increased by 26.4%. However, the share of this expenditure directed to the research of new active ingredients fell from 32.5% to 29.6% (although in actual dollar terms this is a 15% increase). The share of expenditure directed to the development of new active ingredients rose from 23.3% to 24.9%.

- Question 2: Was the observed increase in investment in research on new active ingredients induced by the SPC system?

The data above and the perception of innovators (discussed below) suggest that the SPC framework supported global investment in R&D of new active ingredients in the pharmaceutical and PPP sectors in recent decades.

However, it is challenging to measure the precise contribution made by the SPC framework to the increase in global R&D efforts, and specifically to R&D with the potential to generate new active ingredients in the EU. This is because other factors can also have a significant positive or negative influence (see Table 1 below and Annex 9). Quantifying the impact of intellectual property rights on innovation in any field of technology is a well-known challenge and the SPC framework is no exception in this respect.

Observing Figure 3 and Figure 4 above, and given the time necessary to develop a new medicine, the surge in US approvals of novel medicines observed between 1994 and 1999 (from around 20 in 1994 to over 50 in 1999) could have been positively influenced by the adoption in 1984 of the US Medicine Price Competition and Patent Restoration Act (Hatch-Waxman Act). This legislation introduced US patent-term extensions (the US version of the EU's SPCs) along with other measures (e.g. a five-year period of data exclusivity, and the establishment of the 'Orange Book' where the US FDA publishes the patents that originators believe cover their approved medicines). South Korea and Japan introduced patent-term extensions in 1987 and 1988 respectively.

Table 1 below shows factors that: (i) help increase or hamper global R&D investment in the pharmaceutical and PPP sectors, and (ii) have arisen in parallel to the introduction of SPC protection in the EU. Negative factors may have encouraged investment in incremental innovation, such as the repurposing of known active ingredients and increasing reliance on follow-on patent protection such as secondary-medical-use patents.

Table 1: Factors influencing the allocation of investment in pharmaceutical and PPP R&D in the EU

Factors that positively influence investment in global R&D for new active substances	Factors that have a negative impact on investment in global R&D and new active substances
- IP protection in the EU and other countries[33] - Regulatory incentives such as data and market protection, orphan incentives and paediatric rewards[34] - Growing global demand[35] for pharmaceuticals (over EUR 1 tn annual expenditure with over 6% annual growth) and greater expenditure on medicines[36] - New technologies that have untapped new treatment opportunities (e.g. biotech) - Increasing public[37] and private funding in pharma. This is facilitated by IP rights like the SPC, as IP rights can be used as loan/funding collateral and facilitate licensing and outsourcing	- Increasingly stricter regulatory requirements, including post-approval requirements. These are especially discouraging for the PPP sector. They may have encouraged: (i) investment in incremental innovation like the repurposing of known active ingredients; and (ii) increasing reliance on follow-on patent protection such as secondary-medical-use patents (see the pharmaceutical-sector inquiry launched by the European Commission in 2008). - High cost of new techniques to develop new substances[38] - Mergers of leading companies[39]

33 The MPI (2018) and Kyle (2017) studies discuss how pharmaceutical innovation is financed from global profits. The US market (representing 64.1% of the global sales of new medicines launched in 2012-2017 according to the EFPIA data centre) has experimented a significant increase in medicine prices. It has also introduced IP, regulatory and tax incentives for pharmaceuticals (the 1984 US Medicine Price Competition and Patent Restoration Act), arguably encouraging additional investments in pharmaceutical R&I. Likewise, Korea and Japan introduced patent-term extensions in 1987 and 1988 respectively.

34 SWD(2020) 163 final.

35 Deloitte report, 2020 Global life sciences outlook (2020) https://www2.deloitte.com/global/en/pages/life-sciences-and-healthcare/articles/global-life-sciences-sector-outlook.html.

36 e.g. Giaccotto, C., Santerre, R. E., & Vernon, J. A. (2005). Medicine prices and research and development investment behavior in the pharmaceutical industry. *The Journal of Law and Economics*, *48*(1), 195-214.

37 Iain M Cockburn, Rebecca M Henderson, 'Publicly Funded Science and the Productivity of the Pharmaceutical Industry' in Adam B Jaffe et al., *Innovation policy and the economy* (MIT press 2001) p. 21.

38 In the 1990s the pharmaceutical industry allocated between 10% and 15% of its turnover to R&I, but in 2017 the industry reported spending over 20% of its turnover on R&I.

DiMasi et al. (2016) estimates that the cost of bringing a new medicine to the market is now over USD 2 billion. However, other researchers' estimates conclude that the cost might be substantially less than the estimates by DiMasi et al. (e.g. Olivier J. Wouters, Martin McKee, Jeroen Luyten (2020). 'Estimated research and development investment needed to bring a new medicine to market, 2009-2018'; [published March 3, 2020] *Journal of the American Medical Association*). Wouters, McKee and Luyten estimated the average investment to bring a new product to market at USD 985 m (accounting for costs of failed trials).

The overall R&D costs for a new PPP have increased from USD 152 million in 1995 to USD 286 million during the 2010-2014 period (Phillips McDougall and Deloitte).

39 Both sectors have seen a continuous wave of mergers. The concentration of major companies is more acute in the PPP sector where, in 1996, 12 companies held approximately 35% of global market share, with only 6 companies controlling 60% of the PPP market in 2011. The pharmaceutical ecosystem has many innovative start-ups. The register of the EMA's 'SME office' contains over 1 500 companies registered as active in the

Stakeholders' perception of the impact of SPCs on innovation

The Commission's public consultation asked innovators (see Section 2.3 above) some questions about the role of the SPC system in their own innovation-related decisions. Their answers (71 respondents) appear to reflect the SPC's positive impact as detailed below. However, it can also be observed that many of the respondents did not answer some questions.

Thus, question 6 asked: For innovative products or potential innovative products, does the possibility of getting EU SPC protection play a role when your company/organisation is deciding on the following investments? (i) in R&D (excluding clinical/field trials) and (ii) in clinical trials (medicinal products), or field trials (for plant protection products). In their answer to Question 6(i), only 4 out of 71 innovators answered 'No', with 32 reporting that SPC protection had a positive effect. However, 45% of innovators (32 out of 71) did not provide a reply. In their answer to Question 6(ii), only 1 out of 71 answered 'No', with 33 reporting that SPC protection had a positive effect. However, 45% of innovators (32 out of 71) did not provide a reply.

The Commission public consultation also surveyed other stakeholders (see Section 2.3 above). Here, the Commission asked patients, farmers, health practitioners and health-related authorities how they perceived the progress made in the last two decades in the EU for investments in pharmaceutical innovation and PPPs in general. In their answers, 10 out of 15 stakeholders reported a positive trend, with 2 reporting a stable trend, and only 1 reporting a negative trend. These questions were also included in the questionnaire addressed to industry players, innovators and trade authorities, who replied as follows (only 5 replies were received, which is a limited sample): 2 out of 5 reported a positive trend, with 1 reporting a stable trend, and 1 reporting a negative trend.

The Commission public consultation did not address specific questions on innovation to makers of generics as these companies are not expected to invest in new active ingredients. However, the issue of generics was addressed in the Allensbach survey for the Max Planck Institute (MPI) study contracted by the Commission, discussed in the following paragraph.

Further surveys show that SPC protection appears to be highly coveted by innovators, including SMEs[40]. The Allensbach survey (Question 26) found that 80% of respondents agreed/strongly agreed with the statement that the current SPC regime fosters investment in R&D activities, with only 15% of respondents disagreeing or strongly disagreeing. Around 65% of respondents from the generics industry agreed/strongly agreed with that statement. The Allensbach survey also found that more than two thirds of all industry respondents agreed or strongly agreed with the statement: 'the current SPC Regulations act as an incentive to develop more products for which a longer time is needed until a marketing authorisation is obtained', while 19% of the respondents disagreed or strongly disagreed.

However, not all researches supports the claim that the SPC Regulations made a critical difference. Research[41] conducted by Médecins Sans Frontières that focused on three best-

pharmaceutical sector in the European Economic Area (EEA) with SME status. This represents a sharp increase in recent years (10 times more SMEs than in 2006)).

40 As reported by industrial associations like EuropaBio and European Biopharmaceutical Enterprises (EBE), which represents the interests of biopharmaceutical companies in Europe (60% of its members are SMEs).

41 Hu, Y., Eynikel, D., Boulet, P. *et al.* Supplementary protection certificates and their impact on access to medicines in Europe: case studies of sofosbuvir, trastuzumab and imatinib. *J of Pharm Policy and Pract* 13, 1 (2020).

selling medicines concluded that the internationally accepted patent term of 20 years would have been sufficient to recoup the R&D investments related to those three medicines, claiming that the assumed general need for SPCs is incorrect, at least for some medicines. In this regard, it is accepted that the time needed to recoup investments for developing a particular medicinal product may depend on several factors and be shorter for some medicines, e.g. blockbusters. Annex 4 makes calculations in this regard for a large sample of medicines.

In the veterinary sector, innovators consider any existing incentive, including the SPC, as necessary for investment in innovation, especially given the challenges described in the impact assessment accompanying the Commission proposal on Regulation (EU) 2019/6 on veterinary medicinal products[42].

5.1.2 Objective 2: Attracting R&D to the EU and preventing delocalisation

Another objective of the SPC Regulations prominently claimed by the legislators was to promote R&D activity within the EU, and consequently to prevent the delocalisation of research centres and related jobs to non-EU countries.

- Question 3: Have more pharmaceutical and PPP investments and jobs in R&D been brought to the EU since the introduction of the SPC? How have those investments developed in other trading partners of the EU?

Pharmaceutical sector

In 1992, pharmaceutical R&D and manufacturing was essentially located in the US, Western Europe and Japan[43]. Today, R&D and manufacturing for pharmaceuticals[44] and PPPs are global phenomena, with increasing global competition to attract investment.

Despite this increasing global competition, the EU pharmaceutical industry remains a leading sector in R&D investment. The innovative pharmaceutical industry alone invests over €37 billion in research in Europe, the highest proportion of all industrial sectors, with 795,000 direct jobs[45] and a €110 billion trade surplus (2019)[46]. According to Eurostat, the pharmaceutical-manufacturing sector (NACE Division 21[47]) in the 27 Member States of the EU (EU27) is characterised by a small number of very large, capital-intensive enterprises..

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42 That impact assessment highlights that 'since 1991 the costs for new product development (total costs from discovery to first sales, including application procedure) have risen by 229% for food-producing animals, 173% for companion animals and 108% for minor species. The cost of developing a regulatory dossier which would meet European requirements for a major species has been estimated at 15-50 million euros, while for an additional indication it has been estimated at 2-6 million euros'. Surveyed stakeholders complained about the regulatory burden faced when developing and registering innovative medicines.

43 Gambardella, A., Orsenigo L., & Pammolli, F. (2000), Global competitiveness in pharmaceuticals: a European perspective, available at https://mpra.ub.uni-muenchen.de/15965/1/MPRA_paper_15965.pdf.

44 See table on page 42 at: https://www.ifpma.org/wp-content/uploads/2017/02/IFPMA-Facts-And-Figures-2017.pdf

45 European Federation of Pharmaceutical Industries and Associations (2020) The Pharmaceutical Industry in Figures Key data 2020 (https://www.efpia.eu/media/554521/efpia_pharmafigures_2020_web.pdf)

46 Eurostat – International trade in goods by type of good (https://ec.europa.eu/eurostat/statistics-explained/index.php/International_trade_in_goods_by_type_of_good) .

47 Manufacture of basic pharmaceutical products and pharmaceutical preparations.

According to the EFPIA[48], the average annual growth rate of pharmaceutical R&D within the EU was 4.6% from 2000 to 2015. Figure 8 and 9 below depict a significant and sustained increase in pharmaceutical R&D in the EU since the introduction of the SPC for pharmaceutical products. Figure 10 shows growth in European employment in pharmaceutical R&D since the introduction of the SPC protection.

On the development of investment in pharmaceutical R&D, US-based investment in pharmaceutical R&D clearly outperforms that of the rest of the world[49] (See Figure 9). The EU is the second largest base for R&D investment at global level, with China increasingly closing the gap[50]. A study by Grabowski and Wang (2006) found that the EU maintained a leading position in the generation of NCEs from 1982 to 2003 (Figure 11), after which time the USA caught up and is now in the lead. Indeed, more recently, 83% of the new medicines approved by the US FDA between 2017 and 2018 originated in the USA[51].

Spending on pharmaceutical R&D in China grew at an average annual rate of 21.5% between 2008 and 2015. China does not provide for SPC protection[52], but it benefits from large State-driven investments in R&D and from foreign R&D investment attracted by its immense and growing demand for medicines.

On employment trends, the CE study noted that, although employment within pharmaceutical R&D within the EU increased by 49% between 1990 and 2015, overall employment within

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48 A PricewaterhouseCoopers (PwC) study on the economic and societal footprint of the pharmaceutical industry in Europe, contracted by the EFPIA said the following: 'The pharmaceutical industry is a major contributor to the European economy. We estimate that in total, it contributed €206 billion in gross value added (GVA) and 2.5 million jobs (642 000 direct jobs, 780 000 indirect jobs and 1 072 000 induced jobs) in 2016, equivalent to 1.4% of the EU's combined GDP and 0.9% of the region's employment. The largest contributions are made in Germany, the United Kingdom and France. As well as supporting a significant number of jobs, the industry has been making strides in areas of representation and gender equality and compares favourably with other key industries. In 2016, 46% of the pharmaceutical industry's workforce were women.' This study states that the pharmaceutical industry directly contributes an average of EUR 156 000 of GVA for every employee, which is significantly higher than the EU average (EUR 59 000), or the average for the car-manufacturing industry (EUR 85 000) or aerospace manufacturing (EUR 102 000).

A survey by the EFPIA of its corporate members in 2019 showed that 35% of respondents reported an increase in their investments in the EU over the past 3 years, with 51% of respondents reporting no change. The EFPIA argues that R&I and commercial segments of the value chain seem to have benefited the most from this positive trend.

49 The Commission explanatory memorandum for the proposal for the SPC Regulation reported that during the 1980s there was a decline in the number of molecules of European origin that reached the R&I stage, from 65% to 40%.

50 See page 36 of the study *Biotech in Europe, Scaling Ion, McKinsey, 2019.*

51 Taking the 15 highest-selling medicines in 2018, only 2 were commercialised by an EU company (and these two were jointly commercialised with US partners). A Swiss company was responsible for the commercialisation of 3 of those 15 medicines, and US companies were responsible for the commercialisation of the remaining 10 (including the top 6).

52 On 17 October 2020, the 13th Standing Committee of the National People's Congress of the People's Republic of China adopted amendements to the patent law of China, including the possibility for patent holders to request up to five years of patent term adjustment for invention patents related to "new drugs" that have been approved for marketing in mainland China (art. 42, para. 3). However, this term adjustment is not equivalent to an SPC as the former only compensate for the time taken by the Chinese medicine agency for the review and approval of a new medicine.

the pharmaceutical sector did not increase between 2006 and 2014. Moreover, employment in R&D between 2010 and 2015 in the EU decreased (Figure 10).

Figure 8: Development of R&D expenditure in several geographical areas

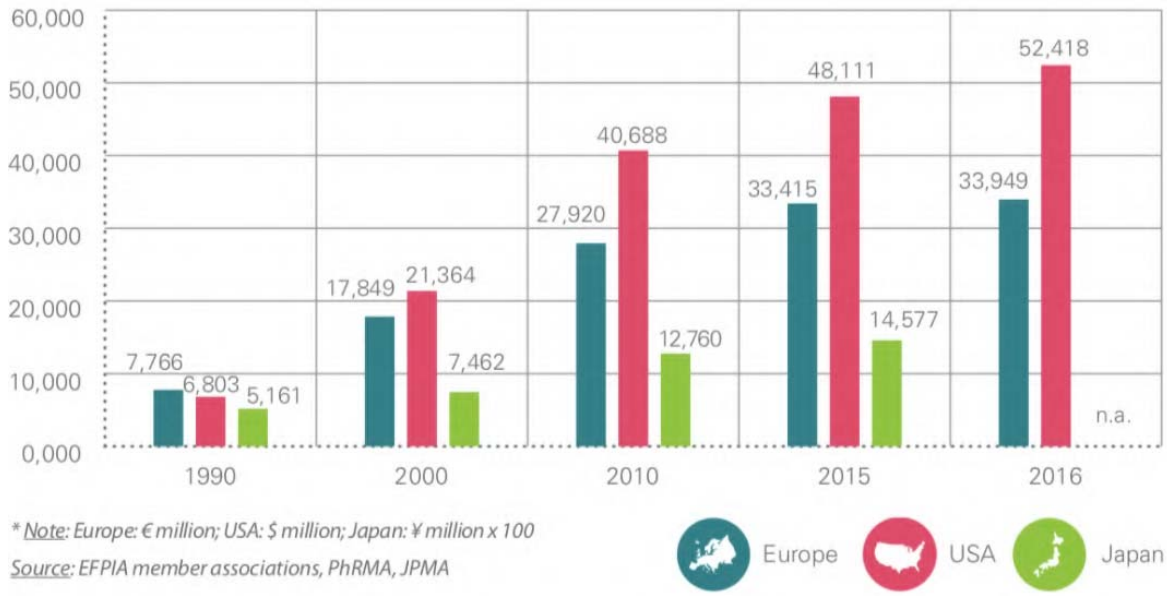


Figure 9: Change in business enterprise pharmaceutical R&D (BERD) in the EU and USA relative to 1975 (Source: OECD)

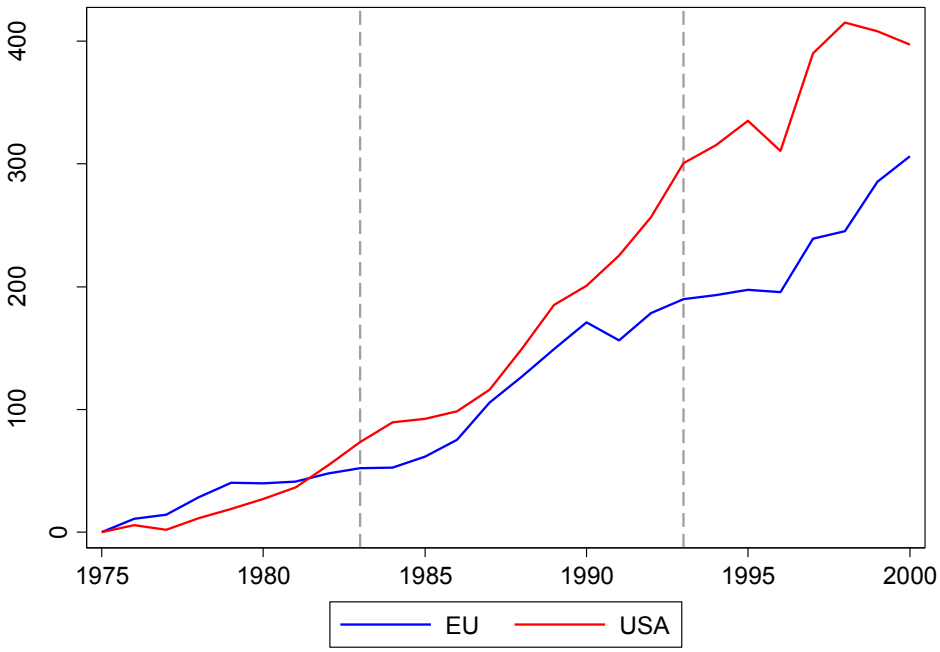
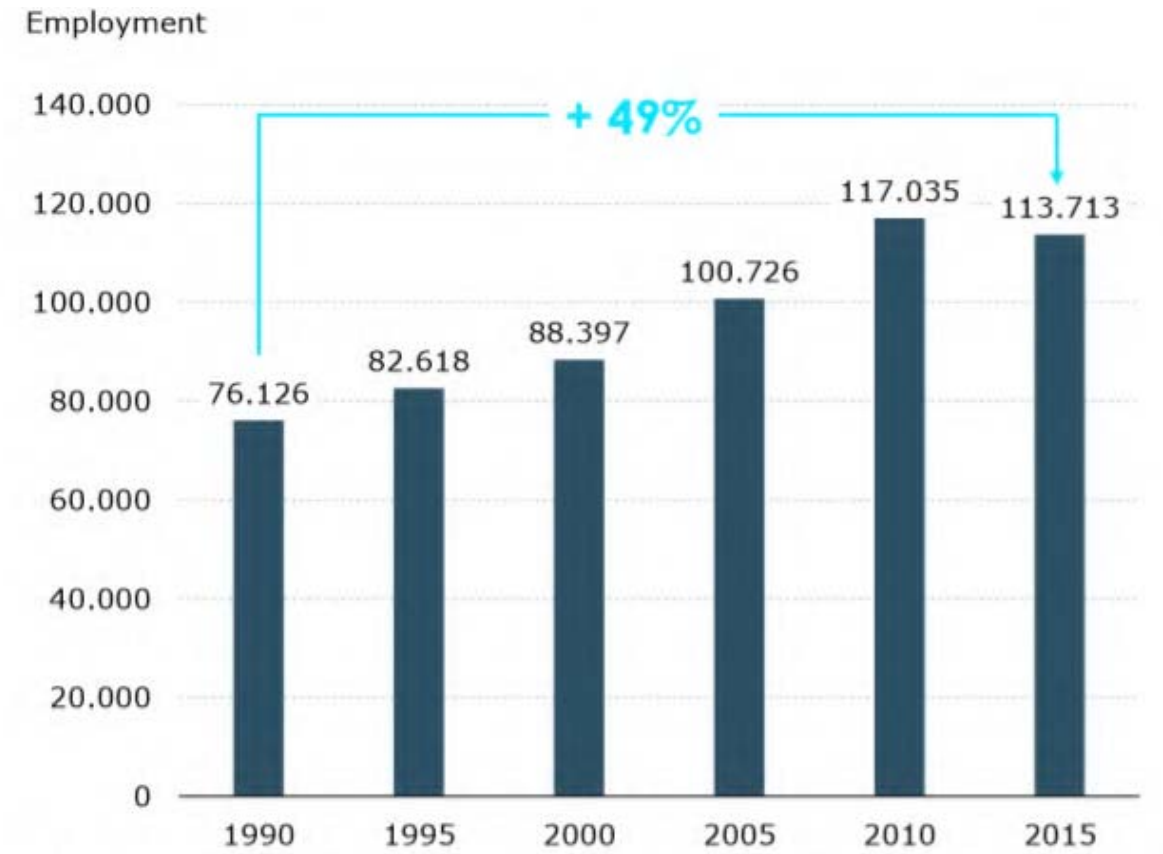
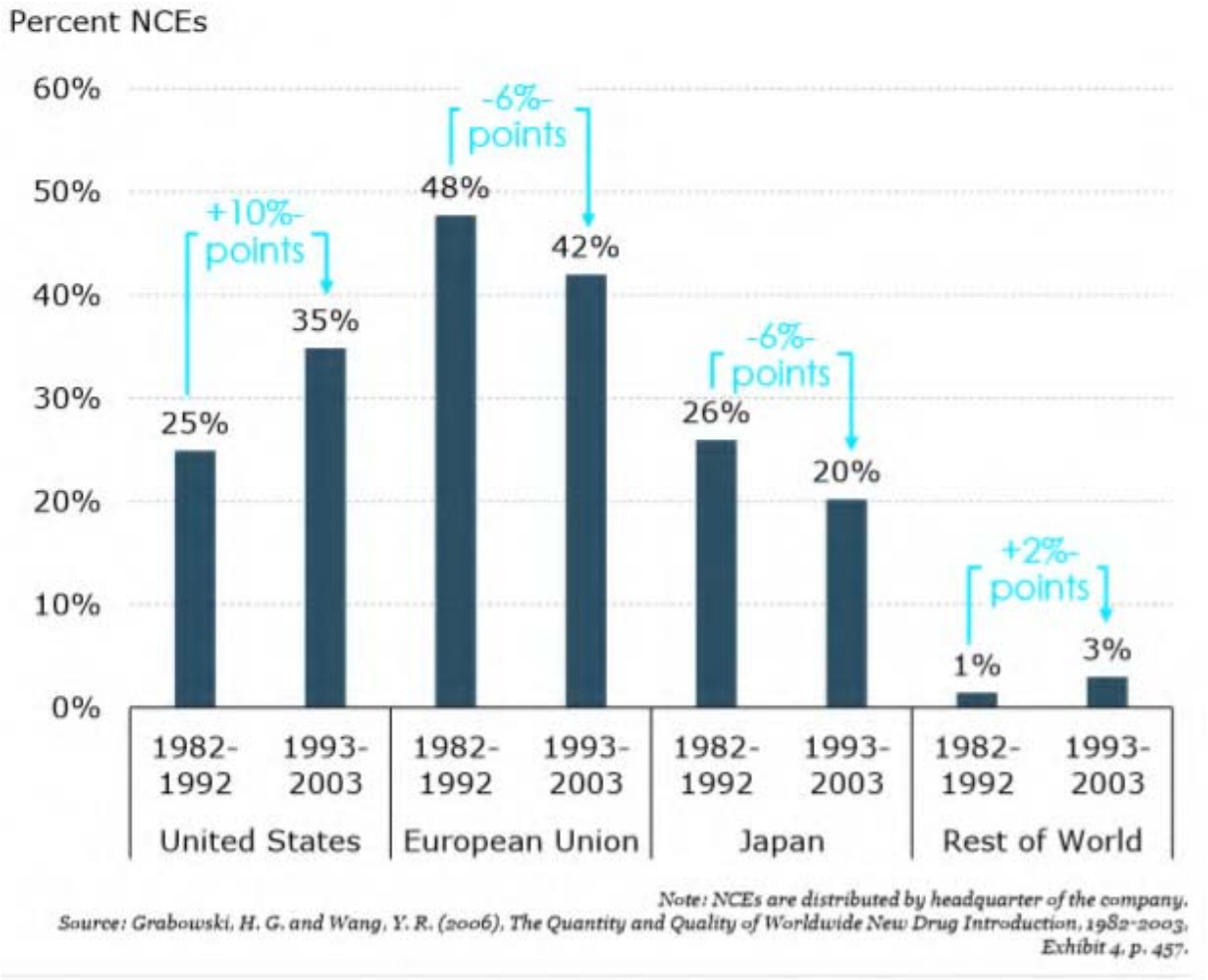


Figure 10: Changes in employment within pharmaceutical R&D in Europe (CE study of 2018)



Note: Data includes Greece & Lithuania (since 2013), Bulgaria and Turkey (since 2012), Poland (since 2010), Czech Republic, Estonia and Hungary (since 2009), Romania (since 2005) and Slovenia (since 2004).
Source: EFPIA based on member associations, available at https://www.efpia.eu/publications/data-center/the-pharma-industry-in-figures-employment/employment-in-pharmaceutical-rd/

Figure 11: Geographical distribution of discovery of NCEs (CE study of 2018)



Note: NCEs are distributed by headquarter of the company.
Source: Grabowski, H. G. and Wang, Y. R. (2006). The Quantity and Quality of Worldwide New Drug Introduction, 1982-2003, Exhibit 4. p. 457.

For the veterinary sector, the impact assessment[53] accompanying Regulation (EU) No 2019/6 on veterinary medicinal products provides a detailed account of the sector's current circumstances and the challenges in developing medicines for veterinary use. It noted that the sector directly supports 50 000 jobs in Europe and over 100 manufacturers.

PPP sector

The EU PPP industry remains a global leader in R&D and manufacturing, with the emergence of new players in Asia where demand and the industry are growing steadily. In 2012, Asia overtook Europe as the largest market worldwide for PPPs.

In 2018, European countries exported USD 17.6 billion of pesticides (48.2% of global exports – noting that this figure includes Switzerland, which was the origin of 0.8% of the global exports). In second place, Asia exported USD 12.3 billion (33.7% of global exports), with China alone exporting USD 5.3 billion. In third place was the US, with USD 4.2 billion in

53 https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52014SC0273

exports[54]. Following a wave of mergers among the major companies in this sector, two German companies remain among the now reduced number of major global groups[55].

- Question 4: To what extent did the SPC Regulations increase investments in pharmaceutical and PPP innovation in the EU?

Measuring the role of the SPC in the overall increase of R&D efforts by the pharmaceutical and PPP sectors within the EU. This is because several factors influence the geographical distribution of R&D activities. Many of these factors are as powerful now as they were in 1992, but others have emerged since then.

The difficulty of measuring the role of the SPC in this area is reflected in the response to the Commission public consultation. Over 60% of the 71 innovators that participated in the Commission public consultation did not reply to Question 9, which inquired about the most relevant drivers 'that affect your decisions on the geographical location/allocation of investments in innovation'. Although 9 respondents reported that the availability of SPC-type protection was among the most relevant drivers, those that did reply to the question mostly reported *other* factors. These replies referred to:

(i) the availability of regulatory data protection (2 respondents);

(ii) the availability of good health infrastructure (e.g. modern hospitals) (5 respondents);

(iii) the proximity of research universities (4 respondents);

(iv) the proximity of an effective regulatory agency (3 respondents);

(v) the availability of public/private funding for their activities (2 respondents);

(vi) labour costs (1 respondent);

(vii) access to high-skilled labour (10 respondents);

(viii) ease of recruiting patients or accessing treatment groups (4 respondents);

(ix) a large market (in terms of potential sales in the country where you decide to invest) (2 respondents);

(x) taxation (1 respondent);

(xi) proximity to the place where the clinical trials (or filed trials) for the product were carried out (1 respondent);

(xii) the possibility of getting 'good manufacturing practices' from the US FDA and/or EMA for the factories based in that country (1 respondent).

The Commission public consultation also asked innovators whether the 'prospective product's eligibility for SPC protection has ever been a decisive factor in its development (i.e. without an SPC you would have discarded it despite having already invested in part of its development)?'. 33 innovators responded positively to this question, confirming that eligibility for SPC protection was decisive in their product's development. There was then a follow-on question: 'Was the prospective product being developed (or did most of its

54 http://www.worldstopexports.com/top-pesticides-exporters/

55 http://images.intelligence.informa.com/Web/InformaUKLimited/%7Bb9c5dc16-821f-44ac-8396-60f28bb66a28%7D_PMcD-Evolution-of-the-Leading-Agrochemical-Companies-v4-2019-ONLINE.pdf

development take place) in the EU?'. Of the 33 innovators who responded positively to the earlier question 51% (i.e. 17 out of 33) replied 'Yes' to the follow-on question and only 1 replied 'No'.

The European Biopharmaceutical Enterprises (EBE), which represents the interests of biopharmaceutical companies in Europe (60% of its members are SMEs), reported to the Commission as part of the SPC public consultation. Its report said that any legal uncertainty around SPCs had the potential to deter investment, postpone development decisions and undermine Europe's reputation as a safe haven for research and development. The EBE said that any uncertainty would particularly impact EU-based pharmaceutical SMEs and start-ups, which have fewer resources to undergo lengthy development pathways for their products (they rely on the prospect of getting patent protection and a subsequent SPC). Specifically, for the veterinary sector, the impact assessment accompanying the proposal for Regulation (EU) No 2019/6 on veterinary medicinal products points out several factors that influence decisions on the geographical localisation of R&D. These factors are strongly influenced by market forces (e.g. a massive increase in demand for animal-origin food and companion animals in Asia) and regulatory approaches outside the EU.

According to the CE study, companies geographically allocate their R&D activities not only on the basis of IP rights but also according to a number of other criteria, such as the availability of a qualified labour force, good health infrastructure, easy recruitment of patients for trials, research universities, public private partnerships, tax schemes, R&D subsidies, high spending on pharmaceuticals or PPP, etc. For many of those factors (some of which fall under national competences in the EU) the USA clearly outperforms the EU (e.g. the USA has higher expenditure on medicines and greater funding available for start-ups through their whole cycle of development).

The MPI and Kyle studies also recall that companies conducting their R&D activities outside the EU can benefit from the IP protection available in the EU and in non-EU jurisdictions. Kyle study (2017) finds that almost 44% of SPC applicants are US-based companies, with Japanese and Swiss-based applicants accounting for 7% and 6%, respectively. Overall, these figures reflect the geographical distribution of R&D.

Replies to Question 26a of the Allensbach survey for the MPI study show that 36% of stakeholders agreed that the SPC Regulations prevented the relocation of research centres outside the EU and 34% disagreed. There was a large division between originator and generics companies on this question, as 57% of originator companies agreed that the SPC Regulations prevented the relocation of research facilities outside the EU, whereas only 19% of generics companies shared this opinion.

In 2019, the EFPIA launched a survey of 18 of its corporate members, as part of the PwC study on the influence of IP incentives (SPCs, regulatory data protection, orphan market exclusivity, and paediatric rewards) on their investments in the EU. Respondents identified IP incentives, followed by quicker market access, as the leading factors influencing their R&D investment decisions. The survey concluded that phasing out existing IP incentives in the EU over a period of 5 years would have a negative impact on their European operations and on EU research-based investment activity in particular. Half of the respondents stated that this scenario would lead to a reduction in their R&D and commercial footprints of more than 25%, and that they would seek opportunities in other regions.

For the PPP sector, the discussion earlier on in this report raised the possibility that other factors external to the SPC have offset the positive effect of the SPC in supporting investment in R&D and in new active ingredients in the EU. These other factors include the maturity of the EU market and the increasingly strict regulatory environment in the EU.

Based on the studies and consultations mentioned above, Annex 9 analyses the strengthens and weaknesses of the EU as a location for R&D investment in the pharmaceutical and PPP sectors.

5.1.3 Objective 3: Promoting a uniform SPC system in the EU

The third objective of the SPC Regulations was to introduce a uniform SPC system at EU level, thereby preventing the uneven development of national laws that would have created obstacles to the free movement of medicinal products and PPPs within the single market.

The lawmakers expected that the SPC Regulations would provide for SPCs granted under the same conditions by each Member State at the request of the holder of a national or European patent relating to a product for which a marketing authorisation had been granted.

- Question 5: Are the SPC grant, enforcement and publication procedures/outcomes uniform across the EU?

5.1.3.1 SPC grant and enforcement procedures across the EU

Respondents to the Commission public consultation (2017) broadly supported (detailed data in Section 5.5 below) the regulation of SPCs at EU level. However, stakeholders claim – and studies and surveys suggest – that the following differences in practices related to the SPC grant and enforcement procedures across Member States have resulted in a fragmentation of the SPC framework:

(1) differences in granting procedures across EU Member States;

(2) differences in the availability/training of SPC examiners;

(3) differences in the length of the examination;

(4) conflicting outcomes of the examinations across EU Member States;

(5) conflicting outcomes in court proceedings.

(1) Differences in granting procedures across EU Member States

Under Article 10(5) of Regulations 469/2009 and 1610/96, Member States may allow the national authority (the national patent office (NPO)) to grant SPCs without verifying that the substantive conditions laid down in paragraphs (c) and (d) of Article 3 (i.e. the requirements that (c) the product has not already been the subject of a certificate, and (d) the marketing authorisation is the first authorisation to place the product on the market as a medicinal or plant-protection product) are met. This has led NPOs to implement different SPC-granting procedures. The MPI study (2018) provides details on the different practices across EU Member States. *In addition, non–examining Member States have produced more grants of SPC, leading to examining Member States referring questions to the CJEU when they wish to refuse an SPC but note that there have been grants elsewhere. The substantive conditions most concerned have been the scope of the patent, but also difficulties to abide by the CJEU's case law on determining which is the first marketing authorisation in the EU.*

The generics manufacturers that responded to the Commission public consultation (2017) mostly (76.19%) supported an SPC-granting procedure that includes a full substantive examination. In this regard, according to a survey conducted as part of the MPI study, most NPOs require an examination of all four substantive requirements stipulated in

Article 3 of Regulation 469/2009. Two NPOs examine only Articles 3(a) and 3(b). Four NPOs replied that they did not examine compliance with the requirement under Article 3(d). However, both the increasing complexity of the state of the art (e.g. the emergence of biotechnology) and the evolution of CJEU case-law have made the examination of SPC applications technically more complex[56]. According to the survey conducted by MPI, some NPOs have declared this growing complexity of the examination to be challenging, especially for NPOs with less administrative resources. However, *Member States have a duty to abide by the CJEU's case law.*

On the role of third parties in the grant procedure, it is noted that the SPC Regulations rule out opposition proceedings[57]. Nevertheless, one Member State has implemented opposition proceedings for SPCs[58]. Furthermore, most NPOs (at least 20) allow the submission of third-party observations, although this is not allowed by at least two NPOs[59] .

As analysed in Section 5.1.3.2, there are also differences in the information published by the various NPOs.

(2) Differences in the availability/training of SPC examiners

The MPI study found that around 8 NPOs had SPC examiners with only a relevant technical qualification and 8 NPOs had examiners with a relevant technical qualification and legal training. In a few NPOs, technical examiners cooperate with the legal department in examining SPC applications.

(3) Differences in the length of the examination

Some stakeholders consulted as part of the MPI study (Question 62 of the Allensbach survey to stakeholders) confirmed that there were significant differences in the length of examination (which can sometimes take more than a year), and expressed their wish for uniform timing and deadlines. Others have criticised the rules in some EU Member States that impose deadlines within the granting procedures. Both originators and generics companies highlighted the importance of a quick decision on a product's eligibility for an SPC. These differences between the procedures in different countries may even be detrimental to the accessibility of generic products. This is because generics makers must have early certainty about the extent to which a product may still be protected by SPCs after a certain patent expires (across the EU), in order to make corresponding business and manufacturing plans.

The next point (4) shows data on the backlog of SPC applications across EU Member States.

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56 Some NPOs have introduced their own examining concepts in certain circumstances e.g. the 'core inventive test', extensively discussed starting on page 232 of the MPI study.

57 Opposition procedures enable third parties to challenge the granting of an IP right during the grant procedure (ex-ante opposition procedure) or during a period of time subsequent to the granting of the IP right (ex-post opposition procedure).

58 See MPI study (2018).

59 See MPI study (2018).

(4) Conflicting outcomes of the examinations across EU Member States

In the Commission public consultation, 56.34% of innovator respondents indicated that authorities in different EU countries had taken different decisions on SPC applications for one (or more) of their products. Only 12.68% reported that this had not happened to them. In this regard, 53.97% of generic-maker respondents (and 6 out of 13 SME generic-maker respondents) indicated that authorities in different EU countries had taken different decisions on SPC applications impacting one (or more) of their generics products. Only 14.29% of generic-maker respondents reported that this had not happened to them.

The CE study shows that the system is highly fragmented. In particular, it shows that the share of rejected and pending SPC applications differ to a large degree between EU Member States[60].

Figure 12 below, from the 2015 report *Latest News on Medicinal Product SPCs in Europe* by Alice de Pastors[61], depicts the ratios of pending and rejected SPCs for each EU Member State:

[60] CE study (2018), page 30: 'In Finland, Italy and the Czech Republic, less than 5% of applications are refused, while in Germany, Sweden and Spain, more than 15% of applications are refused'.

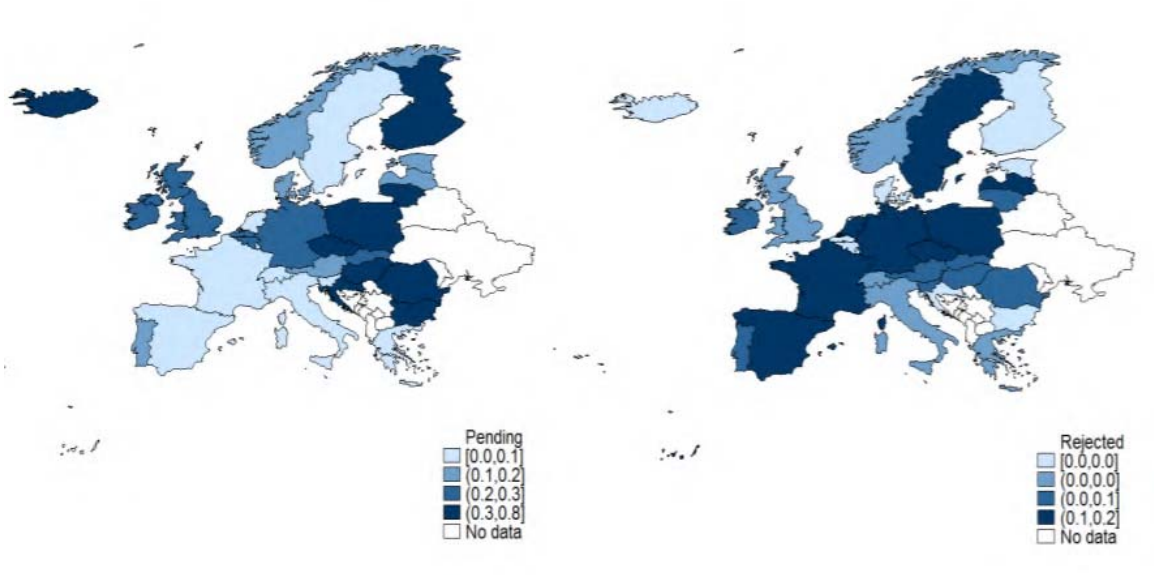
[61] SPC applications pending: discrepancies stem mainly from differences in patent-office procedures such as waiting for decisions by national courts or lengthy proceedings.

- Less than 10% of SCP applications pending: Luxembourg, Malta, Slovenia, Cyprus, Italy, Spain, Portugal, Sweden,
- 10% to 30%: Lithuania, Latvia, Greece, Estonia, Austria, Switzerland, The Netherlands, France, Denmark, Slovakia, Norway, Czech Republic, Ireland, Iceland,
- 30% to 50%: United Kingdom, Romania, Hungary, Belgium, Finland, Germany, Poland, Bulgaria,
- about 97% for Croatia (SPC Regulation entered in force in July 2013).

SPC applications refused: discrepancies relate mainly to different approaches by NPOs.

- Less than 10% of SPC applciations refused: Luxembourg, Malta, Slovenia, Cyprus, Italy, Spain, Portugal, Sweden,
- 10% to 30%: Lithuania, Latvia, Greece, Estonia, Austria, Switzerland, The Netherlands, France, Denmark, Slovakia, Norway, Czech Republic, Ireland, Iceland,
- 30% to 50%: United Kingdom, Romania, Hungary, Belgium, Finland, Germany, Poland, Bulgaria,
- about 97% for Croatia (SPC Regulation entered in force in July 2013).

Figure 12: Ratios of pending and rejected SPC applications in the European Economic Area (CE study and Alice de Pastors)



The differences in refusal rates across Member States suggest[62] that there is scope for divergent decisions on the outcomes of SPC applications. The Mejer study (2017) analyses the outcomes of SPC applications filed between 2004 and 2014 for 706 products. It finds that, for 26% of the products, an SPC was granted in one Member State but rejected or withdrawn in another Member State. Furthermore, the same study found that, in 24% of the cases, SPC expiry dates differ across Member States due to differences in reporting – or interpretation – of the first marketing authorisation date.

According to the Kyle study (2017), there are substantial differences across Member States in the number of SPC applications and the probability of receiving an SPC grant. Since SPC applications may have different outcomes in different countries, efforts to harmonise SPCs across Member States, either through the creation of a unitary SPC or through improved information sharing, would reduce variations in the IP landscape and the uncertainty for generic entrants.

According to the MPI study, inconsistencies and ambiguities resulting from the CJEU's interpretation of central provisions in the SPC Regulations make it difficult for NPOs to adapt their own practices to the criteria set by case-law without causing divergences in relation to either their own previous practices, or the practices of other offices.

The CE study also shows that there are often different outcomes across EU Member States for SPC applications for the same product, i.e. in some Member States an SPC is granted while in others the application is rejected. Similar findings emerged from the Allensbach survey (Question 26)[63]. This fragmentation and its detrimental effects explain why 88% of respondents to the Allensbach survey (both originators and generics companies) expected

[62] The SPC applications corresponding to the same product are not always filed in all EU Member States.

[63] Question 26 was notably about whether respondents agree with the statement: 'When it comes to examining SPC applications, the practice and procedures of the national offices in the EU Member States differ significantly in terms of predictability, transparency and quality of the rights granted.'

a positive impact if 'the procedures for granting SPCs were harmonised within the EU' (Question 59).

(5) Conflicting outcomes of court proceedings

The replies by makers of generics to the Commission public consultation show that 44.44% of generic-maker respondents (and 5 out of 13 SME generic-maker respondents) observed different EU countries making conflicting court decisions related to SPCs that affected one of their generics products. For example, the validity of a generic-maker's SPC was upheld by courts in some EU countries but revoked by courts in other EU countries. Some EU country courts concluded that the generic-maker's products had infringed an SPC while others did not. Originators were also asked the same question. 38.03% of originators saw courts in different EU countries take different decisions on the SPC for one of their products. For example, the validity of an originator's SPC was upheld by courts in some EU countries but revoked by courts in others, or some EU country courts concluded that an originator's SPC had been infringed while courts in other EU countries did not reach that conclusion.

In addition, 33.33% of generic-maker respondents reported that they had conducted multiple defences in a patent/SPC infringement case in multiple jurisdictions (i.e. defences taking place in several EU Member States).

The Commission public consultation shows that 56.34% of the innovators and 61.76% of respondents in group V (i.e. NPOs, judges and IP attorneys) were not satisfied with the length of proceedings for enforcing SPCs, saying that the length of proceedings depended on the EU country.

5.1.3.2 Transparency: publication of SPC-related information across EU Member States

The generics manufacturers that responded to the 2017 Commission public consultation said that the transparency of the current SPC system was not optimal. For example, some respondents indicated that the information published by public authorities was not always comprehensive or up-to-date, and 84.13% of generic-maker respondents (and 11 out of 13 SME generics respondents) stated that access to private databases monitoring SPC status can be costly. Medicines for Europe, the association of generics manufacturers[64], gave the following response to Question 9 of the Commission's public consultation (Question 9 asked how well the original objectives of the SPC Regulations still corresponded to the needs within the EU):

> *From the generics point of view, transparency of SPC granting procedures is of utmost importance. In fact, when applicable, this guarantees possible third party observations or oppositions*. […] *Lack of transparency and of harmonisation brings legal uncertainty. Any possible future SPC system should make sure this is duly considered in order to ensure transparency and predictability for the whole pharma industry* […].

The above response by generics manufacturers was echoed in the response to the Allensbach survey (Question 26), where over 80% of the generics companies agreed that 'when it comes to examining SPC applications, the practice and procedures of the national offices in the EU

[64] Medicines for Europe represents the interests of generics and biosimilar companies in Europe, and they granted consent for the publication of all information in their contribution to the Commission consultation.

Member States differ significantly in terms of predictability, transparency and quality of the rights granted'.

Article 11 of Regulations 469/2009 and 1610/96, which relates to the publication of granted and rejected SPC applications, is not implemented uniformly across EU Member States. According to the MPI study (2018), this impairs the transparency of the SPC system for stakeholders (the degree of transparency was also considered suboptimal in the public consultation). The Commission also launched a survey among NPOs in early 2020 to obtain details on their transparency practices. Based on this survey, the following different practices across NPOs have been identified[65].

- Most NPOs provide an online searchable database, although the search criteria are very variable (in two Member States, the only search criterion that can be used is the SPC number).
- Publishing SPC-related information takes varying amounts of time, ranging from a few days to several months, and even more than a year in specific situations.
- Only a slight majority of NPOs (14 out of 27) publish SPC-related information in English in addition to their official languages.
- Only about half of NPOs make the documents in a file for a given SPC application accessible online (e.g. in PDF format). However, the other NPOs usually allow file inspection and/or are able to provide copies.
- Only a slight majority of NPOs (15) provide the European Patent Office (EPO) with detailed information on SPCs (which the EPO then publishes).
- When asked which source they would consider to be the most suitable for providing centralised access to SPC information, 7 NPOs mentioned the EPO databases (possibly with improvements), 4 did not express any preference, and 14 mentioned a new centralised website.

The above facts are mirrored by the results of the Allensbach survey (Question 26b) for the MPI study: 62% of the respondents (48% of originator respondents and 83% of the generic-maker respondents) to this survey agreed or strongly agreed that the examining practice and procedures of the NPOs differed significantly in the predictability, transparency and quality of the rights granted (26% of the respondents disagreed).

This was also confirmed in a Technopolis study commissioned by the Dutch government (2018)[66].

From this evidence it may be concluded that there is a lack of transparency in SPC-related information. In particular, there is a lack of cross-border transparency, i.e. convenient access to relevant information on all SPCs applied for in respect of the same product in various Member States. Such information relates not only to the filing, examination, granting and maintenance of SPCs, but also to the notification system for the SPC manufacturing waiver introduced in 2019 (Regulation 933/2019), which also has a cross-border dimension. No

[65] This information came from a survey conducted by the Commission in early 2020 among EU Member States' NPOs, in which 24 NPOs participated. Similar evidence is available from WIPO's 2019 survey on patent extensions and SPCs (https://www.wipo.int/edocs/mdocs/classifications/en/cws_7/cws_7_23.pdf). However, this WIPO survey was answered by only 11 EU Member States.

[66] https://www.technopolis-group.com/fr/report/effects-of-supplementary-protection-mechanisms-for-pharmaceutical-products/

evidence is available on the SPC manufacturing waiver, since Regulation (EU) No 933/2019 has only been in force since July 2019.

This lack of transparency in general – and of cross-border transparency in particular – potentially affects both SPC holders and third parties such as generics manufacturers (as further explained in Section 5.2.3 below).

5.1.3.3 Bolar exemption: implementation differs across the EU

All EU Member States have transposed in their national legislation at least the minimum standard of the Bolar exemption as laid down in Article 10(6) of Directive 2001/83/EC and Article 41 of Regulation (EU) 2019/6 (formerly Article 13(6) of Directive 2001/82/EC)[67]. According to the MPI study, in 2018, there are differences in implementation between Member States, which points to incoherence in application of the Bolar provision and can create issues in the internal market[68]. Namely, 5 EU Member States had implemented the Bolar exemption with a narrower scope in comparison with the other 23 that had opted for a broader scope (e.g. covering activities for developing innovative medicinal products and/or for obtaining market authorisation outside of the EU)[69]. The Agreement on a Unified Patent Court (UPC) also includes a provision on the Bolar exemption, which refers to the above-mentioned EU legislation.

There is no Bolar exemption applicable to patents and SPCs on PPPs.

5.2 Efficiency

Assessing the efficiency criterion requires: (i) looking into the costs and benefits of the SPC Regulations for different stakeholders; (ii) identifying what factors are driving these costs/benefits; and (iii) identifying how these factors relate to the SPC Regulations.

As mentioned above in section 5.1.1, the **benefits** of the SPC system are mostly associated with its role in supporting innovation. To quantify these benefits, the evaluation looked into the increase of annual sales for innovators, and the effect of this increase in reducing the risk of not breaking even (i.e. the risk that the additional sales do not compensate for the upfront expenditure in R&D). More innovation is expected to results in the availability of: innovative medicines and new pesticides; more jobs; more industrial and trade activities; and ultimately better health[70]/crops.

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67 Straus, J., 'The Bolar exemption and the supply of patented active pharmaceutical ingredients to generic drug producers: an attempt to interpret Article 10(6) of Directive 2004/27', *Journal of Intellectual Property Law & Practice*, Volume 9, Issue 11, November 2014, pp. 895–908.

68 The Bolar provision is further considered in the Pharmaceutical Strategy for Europe.

69 Table 15.1: Bolar exemption in the EU Member States. As of page 340 of the MPI study.

70 According to the PricewaterhouseCoopers (PwC) study (contracted by the EFPIA) on the economic and societal footprint of the pharmaceutical industry in Europe, pharmaceutical innovation brings about significant societal benefits, as it improves the lives of millions of patients through its contributions to healthcare. The study estimates that: (i) between 2007 and 2017, over 500 000 breast cancer patients received targeted treatments, resulting in a gain of nearly 1.2 million healthy life years; and (ii) new treatments create productivity gains of EUR 9 700 per patient, or EUR 5.3 billion in total, which is equivalent to about 3.5% of the total economic cost of breast cancer care in Europe.

In terms of **costs**, this evaluation looks mainly at three sets of costs, set out below (see summary tables 4 and 6 below).

(1) Costs related to a delay in the market entry of generics.

(2) Costs related to the fragmentation of the SPC system, with granting and enforcement procedures conducted at national level.

(3) Costs related to the suboptimal transparency of the SPC system, which is made worse by both different publication practices across NPOs and the lack of a central up-to-date repository.

5.2.1 Impact of the SPC system on the availability, accessibility and affordability of medicines

The analysis below focuses on medicinal products, but it is also likely to be valid for the PPP sector. However, two major differences must be taken into account. Firstly, consumers of PPPs pay for these products 'out of their own pockets', i.e. there is no social security or public budget supporting the acquisition of PPPs. This is also the case for veterinary medicines. Secondly, there is no Bolar exemption or SPC manufacturing waiver available for companies dealing with generic PPPs.

- Question 6: What is the impact of the SPC on the availability, accessibility and affordability of medicines?

(i) More innovation

The SPC is expected to support innovators in recouping their investments through additional exclusive sales. This would support additional investment in innovation, which benefits society as a whole (i.e. by contributing to greater availability[71] of medicines).

Bearing in mind that the SPC extend on average by 2.5 years the exclusive sales of SPC-protected medicines beyond the regulatory data and market protection (CE study), the cost-benefit analysis of Annex 4 calculates the additional sales that the SPC can add to SPC-protected medicines during the 12.5 years following the market launch in the EU, and concludes that SPC protection adds 13% to the turnover during the first 12.5 years after market launch in the EU when compared to scenario without SPC protection (see also table 2 below). For the analysed sample of 232 active pharmaceutical ingredients (APIs), this additional 13% to the turnover amounts to EUR 37 billion (constant 2018) being transferred from public bodies to innovators. This amount would suffice to cover the cost of R&D for between 39 and 62 new treatments.

As profitability is skewed, half of this impact comes from the top 10% best-selling APIs and markets for these products are shown to be "contestable" (i.e. subject to generics or biosimilars entry when protection expires)

[71] The availability of medicines relies, among other factors explained in this section, on the innovation yield of the pharmaceutical sector. Section 5.1.1 above evaluates the effectiveness of the SPC Regulations in terms of research into new active ingredients. It concludes (see section 6) that the SPC appears to have positevely supported innovation on new active ingredients.

Table 2: Evolution of sales during the regulatory market protection (setting the level of sales in the second year equal to 100 monetary units)

Years since EMA authorisation	Estimated Annual Growth Rate	Annual Sales	Cumulative Sales
2		100	100
3	92%	192	292
4	40%	267	559
5	23%	329	888
6	10%	362	1250
7	5%	379	1629
8	2%	385	2014
9	3%	395	2409
10	0%	**396**	**2804**

Note: DG GROW CET calculations. Annual growth rates for sale years 2-10 are estimated using regression (4.1). The level of annual sales is approximated by putting a value of 100 for sales in second year.

More innovation is expected to bring about greater availability of medicines (innovative as well as subsequent generics or biosimilars), but the availability of medicines is also a function of the speed at which new treatments are approved in Europe. Once a medicine is developed, it must be approved by relevant national medicines agencies in the EU or centrally authorised via the European Medicines Agency (EMA). The SPC does not play a role in the initial approval process for SPC-protected products (the approval process must first be concluded before the SPC application can be filed) and it is not expected to play a role in the approval process for any competing innovative medicine.

On the speed of entry of new active substances (i.e. accessibility of medicines resulting from new active substances), once a medicine is approved by the relevant medicines agency in the EU, generally it must also undergo pricing and reimbursement negotiation procedures with individual EU Member States (pricing and reimbursement of medicines is a national competence). The SPC is not expected to play a role in the duration of these pricing and reimbursement procedures for SPC-protected products or for any other competing innovative medicines.

Other factors clearly play a role in determining the availability of innovative medicines. For example, a study by Kyle in 2019 (see Section 4.1) discusses how other factors external to the SPC, such as the establishment of the EMA, have helped speed up the entry of innovative medicines to the EU. Furthermore, the CE study (2018) states that the presence of R&D activities within the EU promotes the timely launch of medicines. That study describes how pharmaceutical companies often strategically launch their products, EU Member States with large populations and high incomes benefit from more frequent and earlier new drug launches, as do Member States with fewer price controls[72]. The EFPIA's WAIT indicator[73]

[72] In the EU, national authorities are free to set the prices of medicinal products and to designate the treatments they wish to reimburse under their social security systems.

[73] https://www.efpia.eu/media/412747/efpia-patient-wait-indicator-study-2018-results-030419.pdf

shows how negotiation of pricing and reimbursement for both innovative and generic medicines defers the entry of approved medicines by hundreds of days on average in a number of EU Member States, including some of the most populated ones.

The current fragmentation of the SPC system could hamper joint public-procurement initiatives by a group of EU Member States, for example if the SPC scope or duration varied across the Member States that intended to procure medicines jointly. In such procurement situations, fragmentation could thus also hamper market entry.

(ii) Prices and speed of entry of generics

In general, as pharmaceutical exclusivities such as the SPC expire, generic medicinal products[74] enter the market at a significantly lower price than the SPC-protected 'reference' product (generics are 50% cheaper on average) pushing down the price of the original product after generic uptake[75,76]. The SPC, where it expires later than other EU-specific pharmaceutical protections, causes a delay in the entry of generics. Although this is an expected and assumed effect of the SPC that is tolerated to promote innovation, the SPC was also designed with targeted features to facilitate generics' entry onto the market (i.e. the Bolar and manufacturing waiver exceptions).

Section 5.2.2 discusses the adverse impact of the current fragmented SPC system on the generics industry (in terms of cost, predictability, etc.). Furthermore, as discussed below, the entry onto the market of generics can be negatively influenced by a lack of transparency in the SPC granting procedure and status (e.g. uncertainty about which products are protected by SPCs in various EU Member States and for how long).

(iii) Proportionality

Although the SPC system delays the entry of generics, the effects of this delay are expected to be limited and proportionate when compared to the gains from increased innovation.

As already indicated above (see details in Annex 4), SPC protection adds 13% to the total spending on SPC protected pharmaceuticals during the first 12.5 years after market launch in the EU. There is also clear evidence that patients benefit from new treatment that are SPC protected. Yet, by extending protection SPC may impact on accessibility. However, calculations in annex 4 show that the impact is limited to medicines with high profits. Thus, for 25 high profitable active pharmaceutical ingredients (APIs) that saw generics or biosimilars entry, 7.6% more patients could have been treated during 2.5 years in the absence of SPC protection (and if those APIs had been developed).

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[74] Global demand for medicines is increasing, with a significant switch towards generics and biosimilars. This is confirmed by industry data, which show that total global spending on medicines increased from EUR 950 billion in 2012 to EUR 1.1 trillion in 2017, with generics and biosimilars expected to represent 80% of medicines by volume by 2020 and about 28% of global sales (Deloitte, 2018). Sales of generics and biosimilars are estimated to have a future compound annual growth rate of 6.9% (partly due to efforts by governments to contain overall healthcare costs). According to Medicines for Europe, 56% of medicines by volume currently supplied in the EU are generics or biosimilars, with penetration rates varying considerably from one Member State to another.

[75] Report from the Commission to the Council and the European Parliament (2019) Competition Enforcement in the Pharmaceutical Sector (2009-2017), DG Competition available at https://ec.europa.eu/competition/publications/reports/kd0718081enn.pdf

[76] CE study (2018), as of page 144.

As already indicated above (see details in Annex 4), SPC protection adds 13% to the total spending on SPC protected pharmaceuticals during the first 12.5 years after market launch in the EU. There is also clear evidence that patients benefit from new treatment that are SPC protected. Yet, by extending protection SPC may impact on accessibility. However, calculations in annex 4 show that the impact is limited to medicines with high profits. Thus, for 25 high profitable active pharmaceutical ingredients (APIs) that saw generics or biosimilars entry, 7.6% more patients could have been treated during 2.5 years in the absence of SPC protection (and if those APIs had been developed) .

below summarises the findings of the Commission's cost-benefit analysis of the SPC system for pharmaceutical products (see Annex 4).

As already indicated above (see details in Annex 4), SPC protection adds 13% to the total spending on SPC protected pharmaceuticals during the first 12.5 years after market launch in the EU. There is also clear evidence that patients benefit from new treatment that are SPC protected. Yet, by extending protection SPC may impact on accessibility. However, calculations in annex 4 show that the impact is limited to medicines with high profits. Thus, for 25 high profitable active pharmaceutical ingredients (APIs) that saw generics or biosimilars entry, 7.6% more patients could have been treated during 2.5 years in the absence of SPC protection (and if those APIs had been developed) .

- *The SPC system is limited in scope and SPC protection may not be the last protection to lapse*

SPC protection is available only for a limited number of patented medicines (although it is likely to concern a few products that account for a sizeable share of the pharmaceuticals consumed by health systems and patients). Although about 3 000 European patents are granted annually in the field of pharmaceuticals[77], only a few tens of SPC applications are filed every year in Germany (the EU Member State with the most filings). This is due to four main features of the SPC that restrict its eligibility and scope, which are set out below.

(1) Only patents for new active substances not previously authorised are supposed to be SPC-eligible, i.e. only one SPC is expected to be granted per active substance. Recent CJEU jurisprudence[78] (Santen SAS C-673/18, Teva C-121/17 and Abraxis C-443/17) has helped mitigate concerns among generic companies triggered by previous CJEU decisions (especially the Neurim case C-130/11). These decisions could have: (i) altered the delicate balance struck by the SPC Regulations ('one SPC per product' rule); and thus (ii) led to a proliferation of unexpected SPCs and additional delays in the entry of generics[79]. The CJEU has confirmed that new formulations (Abraxis C-443/17) and new indications (Santen SAS C-673/18) of active ingredients authorised in the past cannot be eligible for a new certificate based on a more recent marketing authorisation granted for that formulation or new indication. This is because the more recent marketing authorisation would not be the first marketing authorisation for the active ingredient concerned (i.e. the

[77] CE study (2018), page 26.

[78] See MPI study (2018).

[79] The MPI study analyses in detail the CJEU jurisprudence related to the SPC. An updated analysis of the SPC jurisprudence analysed in the MPI study can be found at: Roberto Romandini, 'Art. 3(a) SPC Regulation: An analysis of the CJEU's ruling in *Teva* (C-121/17) and a proposal for its implementation', *Journal of Intellectual Property Law & Practice*, Volume 14, Issue 3, March 2019, pp. 230-251, https://doi.org/10.1093/jiplp/jpz016.

Abraxis case dealt with a new formulation of 'old' active ingredients, and the Santen case dealt with a new indication for 'old' ingredients. These cases have refined earlier case-law, such as Neurim, on those provisions of the SPC regulations which had provoked the most references). However, the principle of 'one certificate per product' might still not be completely settled in relation to combinations of products, as this principle was based on two pillars, Articles 3(c) and 3(d) of the SPC Regulations. Chapter 12 of the MPI study discusses in detail the potential ways to re-establish this principle (i.e. by correcting the teleological interpretation of Article 3(c)).

(2) Where an SPC is granted for a certain product it may happen that another protection measure expires after the SPC[80] (see Annex 10). A consequence of this is that SPC protection does not always have a decisive influence on the moment from which generics may be placed on the market, and thus on the accessibility and/or affordability of SPC-protected medicines, as other protection measures could apply.

(3) SPC protection cannot prevent the market of competing medicines that are based on different active substances. It allows for competition by innovation.

(4) Only active substances whose development time is more than 5 years are entitled to SPC protection. Development times that go beyond 10 years cannot be translated into an additional SPC term (i.e. the SPC term is capped at 5 years). The Commission's findings, based on data from the Alice de Pastors database, suggest that 45% of the medicines faced a delay of more than 10 years between the filing of the application for a basic patent and the grant of the first marketing authorisation in the EU. This means that the effective protection period of these medicines was less than 15 years. This is consistent with the findings of the CE study (2018) and the Kyle study (2017)[81]. The average duration of the SPC protection in the EU is 3.5 years. Furthermore, according to the CE study[82], in the period between 2010 and 2016 the SPC added on average 2.6 years of protection to products where the SPC was the last protection to expire.

- *The average duration of the effective protection period of medicines is decreasing over time*

The Kyle study (2017) and CE study (2018) studies suggest that the development of new medicines is taking longer and becoming more complex[83]. The CE study concludes that the importance of the SPC for the effective protection of medicinal products has increased over time, in a context where the average 'effective protection period' for medicinal products has been decreasing over time[84]. Therefore, the role of SPCs in ensuring that research-based

[80] Within the dataset of medicinal products built and analysed in the CE study (2018), the SPC was the last measure to expire for 10% of the products, if secondary-medical-use patents are considered (the scope of secondary medical use patents is limited).

[81] Table 7 of Kyle study (2017).

[82] Page 252.

[83] The median number of procedures per clinical-trial protocol increased from 98 to 158 between 1999 and 2005, and the median length of clinical trials increased from 460 to 780 days during the same period.

[84] The CE study stated the following: *When looking at the entire period in our dataset and across all 28 countries where the 558 unique medicinal products have been made available, we find that the bulk of the medicinal products enjoy an effective protection period of between 10 and 15 years. This is the case for 62% of them. Very few (4%) enjoy less. It makes sense that 10 years is a minimum since the [market protection] MP always provides 10 years of protection (the reason that 4% in our dataset enjoy fewer than 10 years of protection reflects the regime prior to the introduction of the MP incentive in 2005). An additional 24%*

industry has market protection of sufficient length to permit recovery of investments appears to have become more important.

- *There are elements built into the SPC system that foster quicker market entry, such as the Bolar exemption and the SPC waiver*

The SPC has been designed and amended to minimise its expected adverse impact on the entry of generics.

Firstly, the SPC is one of the few intellectual property rights the duration of which is not fixed but varies on a case-by-case basis, as explained above, according to each particular situation.

In the field of pharmaceutical products, the SPC protection does not impede the development and registration of competing generics and biosimilars in the EU, because the EU Bolar exemption also applies to SPC protection. In this regard, the CE study states that the Bolar exemption has allowed generics manufacturers to better maintain their activities within the EU because it has allowed research on generics before the expiry of the protection.

Until the recent introduction of Regulation (EU) No 2019/933 on an SPC manufacturing waiver, the SPC was causing unintended adverse effects for EU-based manufacturers of generics and biosimilars seeking: (i) to export to non-EU countries during the SPC term; or (ii) 'day one' entry onto the EU market[85]. Thus, the recent legislation on the SPC manufacturing waiver is expected to also accelerate the market entry of generics and biosimilars in the EU.

- Question 7: Is the maximum duration of the SPC appropriate ?

There are several studies and stakeholders' views on the duration of the SPC.

The Commission's cost-benefit analysis for medicinal SPCs in Annex 4 shows that, for a significant number of active ingredients, the SPC's duration might not be enough to recover R&D investment. Indeed, using information on sales and costs, internal Commission calculations show how many medicinal products break even over 12.5 years (see Annex 4 for methodology) with and without SPC protection. The Commission concludes (see table 3 below) that the SPC might have helped increase the number of medicines that have reached break-even for their investments in R&D by 4 percentage points.

Table 3: Percentage of SPC-protected medicines that break even (Source: Commission's own calculations.)

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enjoy an effective protection period between 15 and 20 years, the 20 years being the original patent protection period. Then comes the last 10%, which enjoy more than 20 years of protection. At first this is surprising as the maximum period of protection is 20 years offered by the original patent. However, the explanation is the existence of the so-called secondary patents. A secondary patent is a patent taken out after the initial patent. The secondary patent is just like any other patent and provides 20 years of protection. But since it is taken perhaps years after the initial patent it effectively pushes the effective protection period beyond 20 years.

[85] Before the SPC manufacturing waiver (Regulation (EU) 2019/933) was introduced, generics makers were prevented from manufacturing and storing generics in the EU (in those Member States where SPCs were in force) until the expiry of the SPCs, with the consequence that these generics were not able to reach these markets for several days or weeks (or months, for biosimilars), while generics made in countries not having an SPC-like protection could be placed on the EU market from 'day one', i.e. immediately after SPC expiry.

Level of medicine development expenditure	With SPC	Without SPC
(low)	42%	38%
(high)	32%	28%

SPC holders claim that the development of new medicinal products has become lengthier and more expensive in recent decades[86]. Associations representing SPC holders that replied to the Commission public consultation warned that a reduction in the term of SPC protection would have a direct negative impact on the ability of SMEs active in R&D and/or manufacturing original products to secure sufficient funding.

Some studies argue that the duration of SPCs is in some cases too generous and even question[87] the need for an SPC framework (as discussed in the analysis of Question 2 above in Section 5.1.1).

The CE study (2018) points out that cutting the duration of the SPC would come at the expense of innovation, especially for product categories where: (i) the requirements for R&D efforts are particularly high; (ii) the diseases are particularly complex; or (iii) the affected stakeholders have limited advocacy power. However, the same study also highlighted that economic theory suggests that, given the competitive status of the market, SPC holders will charge the highest price possible for a longer period, and at the expense of public payers (impacting affordability). The 2018 CE study's statistical modelling[88] suggests a positive relationship between the IP protection period and the level of pharmaceutical R&D in general (i.e. not only on new active pharmaceutical ingredients). This study suggests that when medicinal products are granted a longer effective protection period in the markets where they are sold, pharmaceutical companies increase their innovation efforts. It also concludes that the global reach of medicinal products implies that a reduction of the IP protection period to pave the way for faster entry of generics would negatively affect investments in R&D, both within and outside the EU. However, the same study also noted that *quantifying* the value of the extra innovation (which might be linked to the incentives) is a challenging task.

[86] See reports by Phillips McDougall cited in Section 5.1.1 above for how this discussion relates to PPPs, and the two points of reference of the DiMasi et al. methodology published in 2003 and 2016 for how this discussion relates to medicines. The DiMasi et al. studies of 2003 and 2016 are the most widely cited studies of the cost of developing a new medicine. Comparing both subsequent studies, in the decade from 2003 to 2013, the mean cost of developing a single new therapeutic agent has almost tripled (from USD 1.1 billion to USD 2.8 billion in 2018 USD).

[87] For example, this criticism was raised by Médecins Sans Frontières. See: https://msfaccess.org/briefing-note-supplementary-protection-certificates-spcs.

[88] This modelling has some limitations. It is based on looking at the trade-weighted mean effective protection period (in the EU and USA) with a not very extensive sample, in a context where EU companies that spend a lot on R&D are geographically clustered (trade gravity).

Table 4: Cost - benefit analysis per stakeholder (Source: Commission own calculations, see Annex 4)

Stakeholders	Cost (in EUR)	Benefits (in EUR)	Result
Innovators (SPC users)	Patent & SPC Protection: Patent (EP): EUR 0.15 m SPC (4y): EUR 0.14 m Attorney: (NDA) Litigation (one case): EUR 0.05- 0.2 m SPC search & monitoring: (NDA)	SPC protection adds 13% to the turnover during the first 12.5 years after market launch of a medicine in the EU. For 232 APIs in the sample this amount to a total of EUR 37 051 m. The cash flow increases as market potential (turnover) increases: Median: EUR 55 m Average: EUR 160 m Top 5% selling medicines in our sample: EUR 740 m Top 1%: EUR 1 063 m	The profitability is skewed and half of this additional cash flow is due to the Top 10% of APIs of our sample (in terms of sales).
Generics/biosimilar	Litigation (one case): EUR 0.05- 0.2 m SPC search & monitoring: (NDA)	Introduction of new products creates new markets for generic and biosimilar products.	
Legal profession	Familiarisation with SPC rules and legal system, including cross-border	Litigation (cost per case): EUR 0.1- 0.5 m Attorney fees for managing patents and SPC applications: (NDA)	

Public Authorities and Society	*Patent offices* SPC application account for > 10% of the patent examination workload in small MS and < 1% in largest MS. *Public health budgets* SPC protection adds 13% to the total spending on SPC protected pharmaceuticals during the first 12.5 years after market launch in the EU.	The new medicine launches have reduced years of life lost (YLL) before three different ages (85, 70, and 55) from 34% up to 42%. Furthermore, the introduction of a new cancer medicine in a country was associated with a decline in cancer mortality of 8% for men and 9% for women.[89] Improved quality of life in respect of chronic diseases.[90] Treatment foregone seems to be is limited to high profitable APIs only. For 25 high profitable APIs that saw generics entry, 7.6% more patients could be treated during 2.5 years if there was *no SPC* protection.	Additional cash flow generated due to the SPC would suffice to cover the research and development costs of between 39 and 62 new treatments. Treatment foregone concerns high profitable APIs only.

Note: See Annex 4 for details on the analysis of the impact on innovators (SPC holder) as well as calculations on treatment foregone. Additional sales due to SPC are in relation to counterfactual scenario of having no-SPC protection. See Annex 7 for the workload of national patent offices.

5.2.2 Cost of a fragmented SPC system

- Question 8: What are the costs to stakeholders of the fragmentation of the SPC system?

Costs of fragmentation for SPC users (pharmaceutical and PPP originators)

The SPC framework does not consist of a unitary title granted by a centralised agency and maintained in a single register. In the absence of a unitary SPC, innovators must pursue multiple national filing procedures and pay administrative fees in each EU Member State where they seek protection. Likewise, pending the start of operation of the Unified Patent Court (UPC), enforcement is conducted at national level only.

This fragmentation causes legal uncertainty (as reported by 60 out of 71 innovators responding to the Commission consultation) because grant and litigation decisions can conflict across Member States (see Section 5.1.3).

This fragmentation causes significant additional costs and red tape in getting SPC protection in the EU. For example, 60 out of 71 innovators responding to the Commission consultation agreed (10) or strongly agreed (50) that a unitary SPC would bring less red tape. This is also the conclusion of respondents to Question 62 of the Allensbach survey conducted as part of the MPI study (2018). Those respondents said that the lack of uniformity across Member

[89] Dubois, P., & Kyle, M. (2016). The Effects of Pharmaceutical Innovation on Cancer Mortality Rates.

[90] OECD Health Policy Studies (2018) Pharmaceutical Innovation and Access to Medicines.

States in the SPC-granting procedures – and the results of this lack of uniformity – constitute a serious administrative burden for SPC applicants, and especially for start-ups and SMEs. SPC protection is typically sought in 20 to 24 EU Member States (Kyle and Mejer studies of 2017).

Annex 4 analyses additional costs for the SPC holders for patent and SPC protection in the current fragmented SPC system. It also analyses the cost of enforcing these rights. The cost of patent protection in all EU-27 countries is EUR 152 765, and for SPC protection it is 137 610. This is not including in-house and outsourced patent-lawyer fees (which can largely exceed the administrative fees). For litigation, parties might face a cost of between EUR 50 000 and EUR 250 000 per jurisdiction. This could adds up to a cost of approximately EUR 500 000 for patent and SPC protection (without attorney fees). This cost is relatively small (0.08%) when compared to the lowest overall cost of EUR 600 million for bringing a new medicine to the market, but it can still considerable for EU-based SMEs or universities.

Application and renewal fees for SPCs vary greatly across EU Member States. Table 5 below shows the approximate average total cost of applying for an SPC in all EU-24 Member State[91], and the subsequent annual renewal fees. To these costs must also be added significant additional legal representation costs (outsourcing to specialised patent agents) to conduct the administrative proceedings in each Member State.

Table 5: Cost of SPC filing and renewal in EU-24 as of 2016 (Source: National patent offices' websites; details in Annex 6)

	Application Fees (EUR)	Renewal fees (EUR)				
		1st year	2nd year	3rd year	4th year	5th year
EU-24	7 939	25 787	28 458	31 199	34 045	37 105

These costs are significant for SMEs[92], which have less financial resources, fewer in-house specialists, and limited geographical presence. In this regard, only one patent office in the EU told the Commission's survey on transparency of the SPC system that it provided reduced administrative fees for SPCs to SMEs. Innovative SMEs play a significant role in the pharmaceutical sector. In 2009, the Commission's pharmaceutical-sector inquiry reported that approximately 25% of molecules in clinical development were acquired from other companies, including SMEs. EMA statistics[93] show that 44% (15 out of 34) of priority-medicine (PRIME) applications granted in 2017 came from SMEs.

91 The EU-24, includes the EU-28 Member States but excludes the Member States with the lowest number of SPC applications in 2018, i.e. Croatia, Latvia, Lithuania and Malta.

92 One of the three originator SMEs that replied to the Commission consultation reported that the administrative burden to register and maintain the SPC in all EU countries is high. The other 2 respondents did not comment on this issue.

93 The register of the EMA's 'SME office' contains more than 1 500 companies with SMEs status registered as active in the pharmaceutical sector in the European Economic Area (EEA). This is a sharp increase over recent years (10 times more SMEs than in 2006). There were 185 SMEs registered with a focus on new

In a SPC system with 27 distinct jurisdictions, originators are likely to find it difficult to monitor the use of the SPC manufacturing waiver by generics manufacturers.

Red tape and costs due to fragmentation reduce the positive impact of the SPC framework in encouraging innovation. For example, 52 out of 71 of the innovators responding to the Commission consultation reported that a unitary SPC, i.e. a less fragmented system, would make licensing activities easier. In both the Commission's public consultation and the Allensbach survey (Question 69), a very large majority of the respondents across all categories favoured the creation of a unitary SPC. The CE study (2018) concludes that a scheme like a unitary SPC covering all EU Member States would increase spending on pharmaceutical R&D within Europe.

The fact that the SPC extension reward is granted by independent NPOs makes it difficult for companies to predict whether they will be granted an SPC extension.

In summary, the Commission consultation asked innovators about the advantages of a unitary SPC, i.e. a less fragmented SPC system. The originators (71) were asked if a unitary system would bring:

- a boost to the value of their investments (57 out of 71 agreed or strongly agreed);
- a reduction in red tape relating to litigation (60 out of 71 agreed or strongly agreed; 44 strongly agreed);
- a reduction in red tape relating to registration (60 out of 71 agreed or strongly agreed; 50 strongly agreed);
- increased legal certainty (60 out of 71 agreed or strongly agreed);
- reduced maintenance costs (49 out of 71 agreed or strongly agreed; 45 strongly agreed);
- easier licensing activities (52 out of 71 agreed or strongly agreed).

Cost of fragmentation for manufacturers of generic medicines and PPPs

The fragmentation of the SPC framework causes legal uncertainty for companies dealing with generic products (55 out of 63 makers of generics that responded to the Commission public consultation agreed or strongly agreed that a unitary SPC would bring more legal certainty). This is because SPC grant procedures must be monitored in multiple EU Member States (55 out of 63 generic-maker respondents to the consultation agreed or strongly agreed that a unitary SPC would reduce costs and red tape related to the monitoring of SPC-protected products, i.e. when conducting freedom-to-operate analyses, and enforcement can take place in multiple jurisdictions (56 out of 63 generic-maker respondents to the public consultation agreed or strongly agreed that a unitary SPC would reduce the cost of SPC-related litigation).

Pharmaceuticals and biotechnology patents have the highest litigation intensity across all technical sectors (the sector sees 3 patent cases for every 1 000 patents filed in the aggregate EU-6 (Belgium, Germany, Spain, France, UK and the Netherlands)). In addition, 18% of pharmaceutical patent litigation cases are litigated across borders[94], which entails even higher

formulations/delivery methods, and 256 SMEs specialised in orphan treatments. Pharmaceutical enterprises can apply for SME status at the EMA before requesting financial or administrative assistance from the EMA. The EMA SME register is at: https://fmapps.ema.europa.eu/SME/search_advanced2.php .

[94] Graham, S. J., & Van Zeebroeck, N. (2013). 'Comparing patent litigation across Europe: a first look', *Stanford Technology Law Review*, *17*, 655.

costs (Helmers (2018)). The high costs of litigation directly influence generics makers, with some refraining from launching certain generics solely to avoid any risk of potential litigation that might result from divergent decisions rendered by national courts.

Generics and biosimilars do not enjoy the same scope of Bolar exemption[95] in all EU Member States. Moreover, they can face complex requirements for using the SPC manufacturing waiver (see glossary) if they need to perform cross-border activities (e.g. import of substances or cross-border outsourcing of activities).

As discussed in Section 5.1.3 above, the current fragmentation of the SPC system causes uncertainty in the business plans of makers of generics and biosimilars. For example, it causes uncertainty over whether and when they will be allowed to launch their products in the respective Member States.

In summary, the Commission public consultation asked makers of generics about the advantages of a unitary SPC, i.e. a less fragmented system. 54 out of the 63 generic-maker respondents (including 10 out of 13 SME generic-maker respondents) to the Commission public consultation said they favoured the creation of a unitary SPC for the unitary patent (only 1 opposed). In addition, they were asked if a unitary SPC system would:

- reduce costs and red tape for monitoring SPC-protected products (freedom to operate) (55 out of 63 agreed or strongly agreed);
- reduce the cost of SPC-related litigation (56 out of 63 agreed or strongly agreed);
- increase legal certainty (55 out of 63 agreed or strongly agreed);
- make licensing easier (42 out of 63 agreed or strongly agreed).

Costs of fragmentation for consumers, patients, and (indirectly) health authorities

Fragmentation can have an adverse impact on the availability of innovative medicines, because the uncertainty and high cost of filing patent and SPC applications in multiple EU Member States can lead SPC holders to neglect protection in less attractive EU Member States' markets. This can mean that they postpone launches of their innovative products in those markets (although a number of additional factors, such as national pricing and reimbursement decisions, may also play a significant role). The CE study[96] sees potential in a unitary SPC to overcome this issue. Indeed, 11 out of the 15 respondents to the Commission consultation in the group of patients and consumers of SPC-protected products favoured the creation of a unitary SPC for the unitary patent (i.e. a less fragmented SPC system).

An additional adverse impact is that the current SPC system can hamper the accessibility of medicines. This is because fragmentation and a lack of transparency on the status and scope of SPC protection across EU Member States cause delays in the entry of generics into the EU, especially in smaller national markets. Joint public-procurement initiatives by a group of EU Member States could be hampered if the SPC scope or duration varied across the participating Member States (see the opinion of stakeholders on this issue below).

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[95] The Bolar exemption is regulated at EU level for the pharmaceutical industry only; namely through Article 10(6) of Directive 2001/83/EC and Article 13(6) of Directive 2001/82/EC (replaced by Article 41 of Regulation (EU) 2019/6). The scope of the EU Bolar exemption has been updated in the national legislation of some Member States (e.g. Germany, Ireland and Spain), inter alia to meet new pharmaceutical-related requirements.

[96] e.g. page 224 of the CE study (2018).

The Commission public consultation asked the stakeholders group (consisting of patients and consumers of SPC-protected products) about the advantages of a unitary SPC, i.e. a less fragmented system. They responded as follows:

- a unitary SPC would reduce costs and red tape for monitoring SPC-protected products (freedom to operate) (10 out of 15 respondents gave 4 or 5 points on a scale of 5 (the maximum score) signalling they mostly agreed);
- a unitary SPC would reduce the cost of SPC-related litigation (10 out of 15 respondents gave 4 or 5 points signalling they mostly agreed);
- a unitary SPC would increase legal certainty (11 out of 15 respondents gave 4 or 5 points signalling they mostly agreed);
- a unitary SPC would make joint procurement by a group of EU countries easier (6 out of 15 gave 4 or 5 points on the five-point scale, while 4 respondents gave 3 points on the 5-point scale).

Costs of fragmentation for national patent offices and national courts

In all EU Member States, national patent offices (NPOs) have been entrusted with examining and granting SPC applications, while national courts deal with enforcement[97]. The NPOs charge fees that cover the costs of registration and maintenance of the SPC system. The SPC applications added little workload to the overall workload of patent examiners, especially in large patent offices, considering that on average only a few dozen SPC applications are filed every year. However, it can amount to more than 5% of the patent workload for the NPOs of smaller Member States (Annex 7 for details). In addition, for those NPOs conducting substantive examinations, the complexity of the examination has increased due to the increasing complexity of the state of the art and the CJEU jurisprudence. Many smaller offices seem to have insufficient administrative capacity to conduct substantive examination of the SPC applications[98].

Since each national SPC system can be funded by administrative fees (e.g. SPC application and maintenance fees), the duplication of work does not neccesarily strain public finances. However, this cost is nevertheless borne by the users of the innovation system.

5.2.3 Impact of suboptimal transparency

Suboptimal transparency – and especially suboptimal cross-border transparency – is a major concern at several levels and for several stakeholders.

In particular, the fact that the full file of an SPC application may not be available from certain NPOs (or not available rapidly, or only available in a national language), prevents other NPOs from analysing the reasoning (objections, etc.) of their peers. This hampers the 'informal

[97] The Technopolis study (2018) recommends improvements in the 'proper staffing of patent offices and training of the patent examiners, but also supporting the development towards specialised courts with respective know-how in both IP and regulatory measures'.

[98] The Technopolis study (2018) even mentions 'a shortage of experts with sufficient understanding of both patent and regulatory systems' and says that 'the increased workload entails a risk that – absent reforms to simplify the system – overburdened examiners may opt to just 'rubberstamp' SPC applications without proper scrutiny of the claims.'

alignment' of the various national decisions on identical SPC applications, and thus increases the risk of divergences in the scope of the resulting SPCs.

Furthermore, although the EPO publishes the SPC-related information it receives from NPOs, it appears that only a slight majority of NPOs provide the EPO with such information.

As a result, it is not always easy for generics manufacturers to analyse conveniently the legal situation of a certain medicine across the EU (as regards SPCs). This may create legal uncertainty in certain cases, which may adversely affect the swift entry of generics onto the market, because most generics makers wish to avoid any risk of (very costly) litigation that might result from that legal uncertainty.

The current lack of transparency may also be detrimental to legal certainty for the SPC manufacturing waiver introduced in 2019. This is because this waiver has a cross-border dimension and requires even more clearly that information about the legal situation in other Member States be readily available.

According to the Mejer study (2017) more consistency and transparency would reduce the discrepancies in the scope of protection for originators, and might also improve legal certainty for generic entrants.

The current fragmentation and suboptimal transparency of the SPC system limits the effectiveness of its objectives. It also limits the availability and accessibility of medicines in the EU. By distorting the delicate balance aimed for by the SPC regime between the interests of originators and of generics makers, this hampers the effectiveness of the SPC system, and renders it less fit for purpose than expected (see Section 5.3).

Table 6: Summary table of conclusions on fragmentation and transparency

Stakeholder	Main drawbacks of fragmentation and suboptimal transparency
SPC holders (originators)	- Redundant granting procedures resulting in: (i) legal uncertainty; (ii) additional red tape; and (iii) additional administrative and legal costs. - Redundant litigation and abundant national case-law, which increase legal uncertainty, costs and red tape. - Difficult to monitor the national use of the SPC manufacturing waiver by competing generics/biosimilars. - Uncertainty about obtention of the SPC paediatric extension. These costs could be significant for SMEs, which have less financial resources, fewer in-house specialists and limited geographical presence. Licensing can be more complex to handle. Innovative SMEs play a significant role in the pharmaceutical sector. In 2009, the Commission's pharmaceutical-sector inquiry reported that approximately 25% of molecules in clinical development were acquired from other companies, including SMEs. More recently, EMA statistics show that 44% (15 out of 34) of priority-medicine applications granted in 2017 came from SMEs.
Companies dealing with generic	- Expensive search for – and monitoring of – SPCs in force/or expired in multiple EU Member States. - Monitoring difficulties are exacerbated in the absence of proper

products	transparency (different publication practices across Member States). - Redundant and cross-border litigation – and abundant national case-law – cause increased legal uncertainty, costs and red tape. - Different scope of the Bolar exemption across EU Member States. - Complex use of the SPC manufacturing waiver if cross-border activities (e.g. logistics and outsourcing of production) are necessary. These are especially challenging for SMEs.
Consumers, patients, and health authorities	- Limits the availability of innovative medicines. The uncertainty and high cost of filing patent and SPC applications in multiple EU Member States can lead SPC holders to neglect protection in less attractive EU Member State markets and therefore postpone launches of their innovative products in those markets. A unitary SPC could help overcome this issue. - Adverse impact on the accessibility of medicines. Fragmentation and a lack of transparency on the status and scope of SPC protection across EU Member States cause delays in the entry of generics into the EU, especially in less profitable EU Member States. - Could hamper joint public-procurement initiatives by groups of EU Member States (e.g. where the SPC scope or duration is not the same in all of these Member States).
National patent offices and national courts	- The increasing complexity of the state of the art and the lack of transparency make it more difficult for NPOs and national courts with fewer resources to examine SPCs.

5.3 Relevance

The relevance criterion assesses whether the SPC Regulations are still fit for purpose, i.e. whether the objectives and tools in the Regulations were and are appropriate to tackle: (i) the problems that existed; (ii) the issues that are being faced now; and (iii) the challenges in the near future. The criterion looks at the relationship between the reasons for the Regulations and the current needs and problems in society.

- Question 9: How well do the original objectives of the SPC Regulations still correspond to the needs within the EU (i.e. are the objectives of more innovation in new products, more innovation activities in the EU, prevention of delocalisation, and promotion of a homogenous SPC system in the EU still relevant)?

Our findings show that all the objectives of the SPC Regulation remain relevant and high on the agenda of the EU institutions and Member States.

On objective 1, innovation in the pharmaceutical and PPP sector remains of the utmost importance for society. The fast-growing economies of Asia and Latin America, combined with ageing populations in the EU, USA and Japan, have driven massive global demand for medicines and new treatments in recent decades.

In 2009, the Commission launched an inquiry into the pharmaceutical sector, stating that: 'the lack of adequate treatment for many diseases requires continuous innovative efforts in order to find new medicines. Without the very significant research and development efforts of originator companies and other stakeholders (e.g. universities) these benefits would not be possible'.

In addition, beyond the EU, pharmaceutical and PPP-related innovation provides solutions to the major challenges of the UN's Sustainable Development Goals, such as improving health and the environment or reducing hunger.

The solutions to the current COVID-19 pandemic will be found in pharmaceutical innovations, from diagnostic tests to antivirals and vaccines.

On objective 2, attracting innovation to the EU and preventing delocalisation of EU R&D remain major priorities for the EU, and not only in the pharmaceutical and PPP sectors. Since 1992, the Commission and several EU Member States have repeatedly stressed[99] the need for the EU to further develop its knowledge-based economy with a target of investing 3% of its GDP in research and development to remain internationally competitive. The pharmaceutical and PPP industries remain central to this general innovation objective[100].

The current COVID-19 pandemic has shown the importance of having both R&D and medicine manufacturing in the EU. In this regard, the biologics sector is R&D-intensive, and the manufacturing of biologics tends to be located where R&D takes place[101]. Therefore, any contribution of the SPC to attract EU investment in R&D on biologics might indirectly attract more manufacturing centres to the EU.

It is also likely that the SPC has helped EU-based contracting manufacturing organisations (CMOs) to attract foreign-technology transfer, because foreign innovators can rely on patent and SPCs protection int the EU. For example, the report *Vaccine Contract Manufacturing Market, 2nd Edition, 2019-2030* has the following advice: *it is important to consider the approach to protecting intellectual assets of the country in which the CMO is based.(…)upon outsourcing, the customer company is required to divulge a lot of intellectual property, in terms of development formulas, technologies and protocols, to the service provider… It is also worth highlighting that joint venture companies are generally granted access to certain capabilities and intellectual properties of their parent companies*.

On objective 3, creating a uniform SPC system in the single market remains a major goal for the EU. Pharmaceutical and PPP sectors are cross-border in nature in their supply chains, their research activities (clinical and field trials), and the way they launch their products. One of the three drivers of the Commission's new industrial strategy[102] is about strengthening the single market to improve the EU's competitiveness in the world. Future initiatives to jointly procure

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99 In June 2010, the European Council adopted the Europe 2020 strategy, which included a goal of investing 3% of EU GDP in R&D.

100 Roadmap for a pharmaceutical strategy at: https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12421-Pharmaceutical-Strategy-Timely-patient-access-to-affordable-medicines, and the 2019 European Innovation Scoreboard at: https://ec.europa.eu/docsroom/documents/38781.

101 Alcacer, J. and Delgado M. (2016). 'Spatial organization of firms and location choices through the value chain', *Management Science*, 62(11), pp. 3213-3234. Analysing the locations of new establishments of biopharmaceutical firms in the USA from 1993 to 2005, the authors show that collocation of activities varies in the value chain. Although present in all activities, colocation is greater for R&D and manufacturing than for sales.

102 https://ec.europa.eu/commission/presscorner/detail/en/ip_20_416

medicines by EU Member States can be hampered if SPCs are granted across the EU with different scopes or durations. Some respondents in the group of consumers/purchasers of SPC-protected products responding to the Commission consultation said that a less fragmented SPC system would make joint procurement by a group of EU Member States easier. 6 out of 15 respondents gave a response of 4 or 5 points out of a maximum of 5 points (indicating strong agreement with this assessment), while 4 respondents gave 3 points out of 5 (indicating moderate agreement with this assessment).

- Question 10: To what extent have the original objectives proven to have been appropriate for the SPC Regulations?

The SPC mechanism, broadly speaking, appears to be an appropriate intervention to tackle the objectives of promoting innovation in new active ingredients; and create a uniform solution at EU level. However, the effectiveness and efficiency of the SPC Regulations are undermined by the fact that SPCs are administered and managed at national level and in a very divergent manner (see in particular Section 5.1.3 above). The SPC Regulations themselves appear to have had a limited effect in tackling the objective of attracting R&D to the EU and preventing delocalisation, as other factors have a significant influence on the geographical location of innovation (see Annex 9).

The amendment of Regulation 469/2009 in 2019 introduced an SPC manufacturing waiver (see glossary) that recalibrated the EU intervention. The EU intervention was also recalibrated by the introduction of the Bolar patent and SPC exemption (see glossary) in the pharmaceutical legislation to facilitate the operations of generics and biosimilar manufacturers in the EU. These recalibrations were made to re-balance the interests of innovators and generics makers in the pharmaceutical field.

- Question 11: How well adapted are the SPC Regulations to new technological developments?

The SPC system was introduced to target a specific type of innovation: new active ingredients that required lengthy development periods. This subsection analyses how the SPC system interacts with four other types of innovation.

(1) New models of research into pharmaceuticals and PPPs that are based on incremental innovation (e.g. repurposing of existing molecules to address new and challenging therapeutic areas).

    As discussed in Section 2.2, it was not among the objectives of the SPC Regulations to promote incremental innovation based on existing products, but rather to promote research on new active ingredients. Other IP incentives such as secondary-medical-use patents and regulatory incentives (additional market exclusivity is one such regulatory incentive) are available for incremental innovation. However, an SPC applicant can decide, under certain conditions, to choose a secondary-medical-use patent (and only one) from its portfolio as the basic patent for an SPC application, as long as the active ingredient concerned has not yet been protected by an SPC.

    The issue of the eligibility of SPC protection for incremental innovations has been taken to the CJEU on a number of occasions as analysed by the MPI study (2018). The CJEU decisions confirm that SPC protection is not available for new indications or for uses of known active ingredients (Santen SAS C-673/18).

(2) Since the introduction of SPCs in 1992, there have been major new developments in pharmaceutical and health innovation such as: (i) biotechnology techniques (including

recent gene-editing techniques); (ii) the development of complex molecules, personalised medicines and companion diagnostics; (iii) applied nanotechnology; and (iv) the increasing role of medical devices or 'smart health'.

On biological products, the qualitative interviews conducted for the MPI study (2018) with stakeholders did not reveal significant difficulties in the application of the SPC Regulations to biological medicines. The CJEU has dealt with a number of SPC cases related to biological products. Annex 4 discusses the dynamics of the entry of biosimilars and generics in the market.

The CJEU in case C-527/17 confirmed that SPCs are not available for medical devices per se. However, it is possible to get an SPC for the development of a medicinal product to be incorporated in a medical device. Respondents to Question 40 of the Allensbach survey, when asked whether they would favour or oppose extending SPC protection to other fields of technology, such as medical devices, cosmetic products, or food products and food additives, were divided on the question: 28% supported such extensions, 36% opposed them and 36% found it impossible to say or had no opinion. Out of those respondents favouring an extension to other fields of technology, 91% favoured extending the current SPC protection to medical devices (Question 41 of the Allensbach survey).

Personalised medicines, according to the MPI study (2018), can rely on already known active ingredients protected by second-medical-use patents, requiring an amended or new marketing authorisation. In this regard, and in view of the case law, personalised medicines covered by a second-medical-use patent and which are the subject of a marketing authorisation could be eligible for an SPC provided that the marketing authorisation can be considered as the first marketing authorisation falling under the scope of the basic patent. If the active substance was already authorised as a medicinal product, it is not eligible for further certificates. Therefore, the relevant question is whether the application for a certificate relies on the first marketing authorisation granted for the active substance at issue. The scope of SPC in the EU does not encompass companion diagnostics, with the exception of companion diagnostics that are administered in vivo.

Nano-medicine promises many advances in diagnostics, therapeutics and regenerative medicine. According to the MPI study (2018), although these advances are patentable as a general rule, SPC protection is not available for many of them.

(3) Challenges posed by unmet medical needs[103], including antibiotics[104].

The SPC is an incentive based on prolonging a period of exclusivity of sales. In this respect, it is similar to patents or regulatory market protection. For this reason, the SPC is not expected to be efficient in encouraging research in areas where there is a lack of commercial viability.

[103] See glossary. Unmet medical needs frequently arise where there is a lack of commercial viability for certain medicines, i.e. cases of market failure. This is the case for medicines targeting rare and neglected diseases, and to some extent for antibiotics, which represent a major challenge for the health system (see MPI study).

[104] In response to Question 35 of the Allensbach survey, 49% of respondents opposed an amendment of Regulation 469/2009 in response to the low levels of investment in R&I for new antibiotics. Such an amendment is supported by 23% of respondents.

Some research[105] has proposed the possibility that the SPC granted to a non profitable product (e.g. an antibiotic) becomes a 'wild card' or 'transferrable' SPC that could be applied to extend the marketing exclusivity of other profitable medicines. This has the potential to encourage research in antibiotics. Since June 2018, the US Congress has been considering a bill[106] that proposes a transferable IP-exclusivity extension period to encourage the development of antimicrobial products.

(4) Safeners and PPP SPCs

Safeners are essential to modern agriculture. In cereal crops, for example, more than 80% of herbicides are used in combination with a safener[107] to reduce adverse effects of the herbicide on crop plants, and to improve selectivity between crop plants vs. weed species being targeted by the herbicide. The CJEU, in case C-11/13, accepted safeners as products eligible for SPC protection under Regulation 1610/96.

5.3.1 The COVID-19 pandemic and EU recovery

- Question 12: How well is the SPC Regulation adapted to public health crises, such as the COVID-19 pandemic, and how it can contribute to the EU recovery?

The COVID-19 crisis shows the need for innovative medicines (ranging from repurposing of existing medicines to new vaccine technologies that can be produced in massive quantities in a short period of time). It also shows the importance of keeping R&D in Europe. R&D is often co-located with manufacturing, especially in the biotechnology field.

As shown in recent cases, patents and SPCs have not hampered access to protected medicines for the purpose of conducting emergency clinical trials and tests related to COVID-19. Patent and SPC holders have collaborated with health authorities and researchers[108]. The patent flexibilities introduced for shortages of supplies in health crises (emergency compulsory licences[109] and government patent use) also apply to SPCs.

The SPC regime may not have prevented delocalisation of the manufacturing of innovative medicines and their active pharmaceutical ingredients. However, this was never the SPC regime's intended objective. The focus of the SPC regime was preventing the delocalisation of R&D. The SPC is granted without any condition imposed on the place where the protected medicine, or active ingredient, is to be developed and manufactured.

Improvements in the SPC system that can tackle its fragmentation can help strengthen the EU health and agri-food industrial ecosystems[110] (see Annex 11).

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105 Batista et al., 'IP-Based Incentives Against Antimicrobial Crisis: A European Perspective', published online, 16 January 2019, IIC (2019) 50:30–76.

106 H.R. 6294 REVAMP Act. In this regard, the GAIN and FDASIA Acts have been in place in the USA for antibiotics since 2012.

107 *Zeitschrift für Stoffrecht*, Volume 11(2014), issue 6, pp. 249-252, Frank Gerhards et al.

108 Financial Times, '*Pandemic reopens wounds on IP rights*', 18 June 2020.

109 Financial Times, '*AbbVie drops patent rights for Kaletra antiviral treatment*', 23 March 2020.

110 2020 Commission industrial strategy: https://ec.europa.eu/info/sites/info/files/communication-eu-industrial-strategy-march-2020_en.pdf.

5.4 Coherence

The coherence criterion assesses how well different interventions work together (e.g. in achieving common objectives or as complementary actions). It also assesses areas of tension that need to be identified.

The legal regime of SPCs is complex for two main reasons set out below:

- Unlike patent rights, SPCs have their basis not in national or international law, but in EU regulations that are directly applicable in EU Member States. However, unlike EU trade marks or Community designs, SPCs are not EU [unitary] titles of protection, but national rights administered by national institutions.
- Although SPCs are separate and autonomous sui generis rights, their existence, validity and operation are contingent on the existence of a [basic] patent and a marketing authorisation, which are regulated by laws external to the SPC Regulations.

- Question 13: Are the SPC Regulations internally coherent in their respective provisions?

The existing literature and practice seem to indicate that the SPC Regulations are internally coherent. Regulation 1610/96 on SPCs for PPPs mirrors many provisions and recitals of Regulation 469/2009 on SPCs for medicines (codified version of Regulation 1768/92) (see recital 17 of Regulation 1610/96).

The CJEU has now provided greater certainty on the interpretation of the SPC Regulations and more recently has refined its earlier case-law on those provisions which had provoked the most references. As a result there are now fewer references from national courts.

- Question 14: To what extent is the SPC framework externally coherent with EU legislation on regulatory pharmaceutical legislation, patent law, the unitary patent package and the Bolar exemption? Are there any gaps, overlaps or inconsistencies?

(1) The SPC framework and patent law, including the future unitary patent and the Unified Patent Court

Aspects such as the SPC's duration, expiry and application procedure are linked to its basic patent. The SPC's subject-matter of protection lies within the limits of the protection conferred by its basic patent and its related marketing authorisation(s). On the effects of the SPC, the SPC confers the same rights as conferred by the basic patent. In this regard, Regulation (EU) 2019/933 recently introduced a manufacturing SPC exception for export and stockpiling purposes. However, this manufacturing exemption is not applicable to the basic patent, and only concerns SPCs for medicinal products.

The current SPC system will inevitably inter-link with the future EU patent package establishing a European patent with unitary effect (Regulation (EU) No 1257/2012 and Regulation (EU) No 1260/2012) and a centralised jurisdiction through the Agreement on a Unified Patent Court (UPC)[111]. The future UPC will resolve disputes over: (i) unitary patents; (ii) classic European [bundle] patents; and (iii) related SPCs for those Member States which have ratified the Agreement on a Unified Patent Court.

[111] Details about this international treaty, including its ratification status, can be found at: https://www.unified-patent-court.org/.

Most respondents to the Commission public consultation (2017) were of the view that NPOs would be entitled to grant – under the current legislation – national SPCs for products covered by future unitary patents. According to the MPI study (2018), the SPC Regulations will be coherent with – and complement – the unitary patent system, once the latter enters into force.

(2) The SPC framework and regulatory legislation on pharmaceuticals and PPPs

The issue of the application of regulatory law or of the plant protection product law to supplement the SPC framework is not always simple as analysed by the MPI study (2018). This study recalls that the regulatory framework provides for several types of authorisations and modifications (variations) of existing authorisations, and in this regard the study states that it is not clear whether the *variation* of an existing marketing authorisation can be used to apply for an SPC[112] (i.e. whether it is an authorisation within the meaning of Articles 2 and 3(1)(b) of Regulation 1610/96, or of Article 2 and Article 3(b) Regulation 469/2009)).

It is accepted that centralised authorisations for medicinal products (granted under Regulation 726/2004) can be used to apply for an SPC (i.e. centralised authorisations fall under the scope of Article 2 of Regulation 469/2009).

(3) The SPC framework and the Bolar exemption

The Bolar exemption applies to patents and SPCs for pharmaceutical products. Most EU Member States provide for a Bolar exemption that might be broader than the acts explicitly exempted in EU pharmaceutical legislation[113] (and that will apply to unitary patents under the Unified Patent Court Agreement).

According to the Allensbach survey (Question 65) conducted as part of the MPI study (2018), most (61%) stakeholder groups represented (law firms, associations, originator companies and generic companies) favoured a broad Bolar exemption over a narrow one. Only 18% of the respondents preferred a narrow exemption.

- Question 15: To what extent is the SPC coherent with other EU pharmaceutical and PPP-specific incentives for innovation?

In the EU, in addition to patents and SPCs, regulatory incentives are provided under EU pharmaceutical legislation, running from the date of the marketing authorisation. EU pharmaceutical legislation also provides incentives for orphan medicinal products and paediatric rewards. As explained in the CE study (2018), the regulatory incentives and rewards run in parallel to – and independently from – the patents and SPCs (see Annex 10). The study shows that only 18% of the observations with granted SPCs enjoyed a regulatory data protection period that was longer than their SPC duration.

The SPC framework may not provide sufficient incentives to invest in innovation in some products that have very long development times. However, such innovative products would qualify for regulatory data protection and market protection (see glossary) that guarantee 10

[112] The CJEU in Neurim did not take a position on the question whether a variation of an existing marketing authorisation can support the application for a certificate. This issue was not relevant for the factual scenario discussed in the referal proceedings.

[113] Article 10(6) of Directive 2001/83/EC and Article 13(6) of Directive 2001/82/EC.

years of market protection. The CE study (2018) shows that 18% of the observations with a granted SPC enjoyed a regulatory data exclusivity and market protection that was lengthier than their SPC duration. Therefore, it can be concluded that the SPC and regulatory data protection can complement and mutually strengthen each other.

The SWD on the evaluation of the orphan and paediatric rewards[114] (see glossary) finds that the Paediatric Regulation (Regulation (EC) No 1901/2006) mostly works in a coherent manner with related EU and national legislation and actions. However, the fact that the SPC extension reward is granted by independent NPOs makes it difficult for companies to predict whether they will be granted an SPC extension.

- Question 16: To what extent are the SPC Regulations coherent with international law/obligations?

SPCs constitute a sui generis right that is not directly addressed in the Paris Convention for the Protection of Industrial Property[115] or in the TRIPS Agreement (see glossary), the main international IP-related treaties that regulate the substantive aspects of IP rights at international level. Nevertheless, the obligations stipulated in these treaties may apply insofar as the principles of national treatment, non-discrimination and most-favoured-nation treatment are concerned.

The EU-level SPC legislation has facilitated the inclusion of SPC-related provisions in bilateral trade agreements concluded by the EU. This has increased pharmaceutical and PPP protection in non-EU countries. The provisions in the EU bilateral trade agreements on SPCs were modelled on SPC Regulations 469/2009 and 1610/96.

5.5 EU added value

This subsection aims to assess the additional value brought by the SPC Regulations in comparison to what would have been achieved by the actions of EU Member States alone.

- Question 17: What is the additional value resulting from the SPC Regulations, compared to what would reasonably have been expected from Member States acting at national level?

As discussed in Section 5.1.3 above, promoting a homogeneous SPC system at EU level was one of the main legislative objectives of the SPC legislators (recital 7). Before 1992, only a few EU Member States had adopted national legislation on SPCs. These EU Member States granted national SPCs with significantly different durations.

A number of arguments underpin the value of the EU intervention providing for SPC protection:

(1) medicines and PPPs are developed, tested, approved, produced and marketed along global value chains, with stakeholders favouring uniform, EU-wide regulatory and IP legal frameworks (that could not have been achieved by a bundle of independent pieces of national legislation);

[114] SWD(2020) 163 final.

[115] https://www.wipo.int/treaties/en/ip/paris/

(2) the EU is committed to establishing and ensuring the functioning of the single market with free movement of medicinal products and PPPs (Article 26 TFEU);

(3) the two points above help support patients across borders, who suffer from the same medical conditions and need the same treatments, subject to the same quality and safety requirements (the same applies to farmers in relation to PPPs).

The impact assessment conducted for the proposal for an SPC waiver (SWD(2018) 240 final) states that 'EU-level action would bring significant added value compared to national-level action to the extent that it would preserve the integrity of the single market, by providing for a uniform, transparent and fair approach'.

The Commission public consultation showed that respondents broadly support the way in which SPCs are regulated at EU level. On this issue, an overwhelming percentage of the innovators (80.28%) and a clear majority of generics manufacturers (63.49%) participating in the Commission public consultation considered that the SPC brought added value compared with national initiatives[116] (only 2.82% of the originators and 15.87% of the generics indicated the contrary). 5 out of 15 respondents in the health-user groups replied positively too, with 9 out 15 responding that they did not know. This shows that, from the stakeholders' point of view, legislation at EU level is also the right vehicle to regulate supplementary protection in the pharmaceutical and PPP sectors. However, a number of issues (such as fragmented application) may still need to be addressed – as observed in the responses by innovators and generics manufacturers to the Commission public consultation reflected in Section 5.1.3.1.

The EU legislation on SPCs served as a basis for including SPC protection in bilateral trade agreements agreed by the EU.

6 CONCLUSIONS

This evaluation covers the EU Regulations governing SPC protection for both pharmaceutical products and PPPs[117]. It concludes that both SPC Regulations appear to support research on new active ingredients and are still fit for purpose (i.e. relevant) and coherent with the patent and related pharmaceutical legislation in the EU. Both SPC Regulations appear to have brought EU added value.

However, it is challenging to establish a clear link between SPC protection and the location of R&D, because many other factors unrelated to the SPC play a significant role in the location of R&D. In this regard, as reported by industry associations, patents and SPCs can be especially helpful in supporting innovative EU pharmaceutical companies and in particular SMEs and start-ups, which have fewer resources to embark on lengthy product development cycles.

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[116] Considering both the few actual national initiatives taken before EU legislation was introduced, and the foreseeable consequences of the introduction of additional similar national initiatives in the remaining Member States.

[117] Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products (Codified version), and Regulation (EC) No 1610/96 of the European Parliament and of the Council of 23 July 1996 concerning the creation of a supplementary protection certificate for plant protection products.

The main shortcoming of the existing SPC systems is the fact that SPCs are administered and managed at national level undermines their effectiveness and efficiency. This creates significant red tape and entails extra costs for businesses, especially challenging for SMEs. National grant procedures, including transparency obligations, also entail extra costs and administrative challenges for national administrations (especially for those with reduced administrative capacity). In addition, different approaches and outcomes across EU Member States undermine legal certainty and therefore hamper the proper functioning of the single market. This reduces innovation and the availability of new medicines, and also limits access to affordable generic products, due to the uncertainty faced by generics manufacturers.

In addition, **the overall transparency of the SPC system is suboptimal**, especially in a cross-border perspective. This is detrimental to innovators and generics manufacturers alike.

More specific findings of the evaluation are set out below.

6.1 Effectiveness

The SPC Regulations aim to achieve three objectives: (i) promote innovation for new active ingredients; (ii) attract R&D centres to the EU, thereby preventing delocalisation; and (iii) build a uniform SPC framework at EU level.

The SPC system appears to support research on new active ingredients. There has been growing investment in R&D in the pharmaceutical and PPP sectors as well as increasing approvals of pharmaceutical products – both in the EU and globally – can be observed since the SPC system started. This assessment is also supported by the views of stakeholders. At the same time, the evaluation shows that it is difficult to measure the exact effect of the SPC system on innovation, because decisions to invest and innovate are driven by a large number of factors, including: other regulatory incentives, global demand, new technological breakthroughs (biotechnology), public and private funding, and the regulatory framework in general. An increasingly strict regulatory environment in Europe – for pharmaceuticals but in particular for PPPs – may have offset some of the positive effects of the SPC system on innovation.

Together with other factors, the SPC system appears to have helped attract research centres to the EU and prevent delocalisation of R&D outside the EU. However, limited evidence has been found to support this issue. Localisation of R&D heavily depends on many other factors such as: skilled labour, a sound health infrastructure, life-science universities, the availability of public and private funding, tax schemes, and the level of expenditure on health/medicines in general. All of these factors fall outside the remit of the SPC Regulations. It is likely (and this is confirmed by industry associations) that the prospect of getting SPC protection is especially helpful in supporting innovate EU pharmaceutical SMEs and start-ups when undergoing lengthy development pathways for their products.

The SPC Regulations introduced SPC protection across the EU that is based on a uniform set of rules. However, in practice the fact that SPCs are granted and enforced at national level has resulted in a significant fragmentation. This in turn undermines the efficiency of the SPC system. In fact, there are increasing differences across EU Member States in areas such as the length of procedures, the substantive criteria applied, and the outcomes of the procedures (duration, scope of protection, etc.). The transparency of the current SPC system is also suboptimal, as shown by the evidence gathered. There is no EU-wide information system, and the information published by public authorities is not always comprehensive, up-to-date or

accessible in foreign languages. Moreover, access to private databases that monitor SPC status can be costly, especially for SMEs and start-ups. This has a negative impact on some stakeholders, especially manufacturers of generics.

Diverging practices, suboptimal transparency and the increasing complexity of the technologies make the granting and enforcement of SPCs more challenging, especially for national patent offices and national courts with limited resources. These issues further aggravate the fragmentation of the current SPC framework.

6.2 Efficiency

The benefits of the SPC system are mostly associated with its role in supporting innovation. This is because the SPC increases sales for innovators, and therefore reduces the risk of not breaking even on the upfront expenditure in R&D. More innovation is expected to bring about greater availability of medicines. Other factors can impact the availability of SPC protected medicines in the EU such as the speed of their regulatory approval, on which the SPC has no influence. In the same vain, the SPC has no impact on the duration of price and reimbursment procedures which take place at national level and can significantly hamper accessibility to medicines in the EU. The costs related to the SPC's role in delaying the entry of generics and biosimilars is proportional when compared to the gains from increased innovation. This is because: (i) the SPC has a limited scope (SPCs protect only a fraction of all medicines[118] and PPPs); and (ii) the SPC is often not the last protection to expire (medicines and PPPs also tend to be protected in parallel – during a significant part of their SPC protection – by other EU-specific incentives such as regulatory market protection). For medicines, the effective protection period[119] has been decreasing over time (without SPCs that decrease in protection would have been more acute), and the SPC system provides targeted features to promote the entry of generics. These features include the Bolar exemption and the SPC manufacturing waiver[120].

Additional costs, as mentioned above, stem from the fact that the SPC system is implemented in different ways across EU Member States, with suboptimal transparency. This greatly affects innovators, especially SMEs, start-ups and generics makers (e.g. the cost of monitoring for generics makers), thereby undermining the efficiency of the SPC system.

The current SPC regime therefore appears to ensure that research-based industry benefits from a greater length of effective protection to increase the chances of recovering their R&D investments, without disproportionately delaying the entry of generics.

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[118] The 'products' protected by the SPCs are *active ingredients*. In addition, even for eligible products, SPCs are not granted for products with short development times (less than 5 years), and no additional SCP protection is given for development times exceeding 15 years. On average, a few dozens of products (active ingredients for either medicinal or plant protection products) are the subject of SPC applications each year.

[119] The 'effective protection period' is the time from marketing authorisation until the expiration of the last form of protection in the form of patents, SPCs, or regulatory incentives (i.e. the effective protection period measures the time a product is on the market and enjoys protection from generic competition via either IP rights or regulatory incentives and rewards). The effective protection period for medicinal products has decreased from 15 to 13 years (see page 21 of the CE study).

[120] Introduced by Regulation (EU) 2019/933. See Glossary.

6.3 Relevance

The SPC system remains relevant today. Its key objectives – to promote innovation, prevent delocalisation of R&D and provide for a uniform framework – are of major political importance. The SPC mechanism appears to be an appropriate intervention to tackle the objectives of promoting innovation in new active ingredients and creating a uniform solution at EU level. However, it appears to have had a limited effect in tackling the objective of attracting R&D to the EU and preventing delocalisation, as other factors have a significant influence on the geographical location of innovation.

Innovation in the pharmaceutical and PPP sectors remains of utmost importance for society. The fast-growing economies of Asia and Latin America, combined with ageing populations in the EU, USA and Japan, have driven the global demand for medicines and new treatments upwards in recent decades. Further, pharmaceutical and PPP-related innovation provides solutions to the major challenges of the UN's Sustainable Development Goals, such as improving health and the environment as well as reducing hunger.

The pharmaceutical and PPP industries remain central to the EU's overarching political objective of becoming a knowledge based economy. More recently, the COVID-19 crisis has highlighted the need for Europe to have a strong pharmaceutical sector, and for Europe's pharmaceutical industry to remain a world leader in terms of innovation and manufacturing.

An SPC is granted without any condition imposed on the place where the protected medicine or PPP, or its active ingredient, is to be developed and manufactured. However, examples of the relevance of the SPC (and other IP rights) in supporting manufacturing location decisions has been found: contribution of the SPC in attracting R&D centres for biologics can indirectly attract manufacturing capacity in biologics, and the SPC system (and other IP rights) can help build trust among EU-based contracting manufacturing organisations.

Creating a uniform SPC system in the single market remains a major goal for the EU, because the pharmaceutical and PPP sectors are cross-border in their supply chains, their research activities (clinical and field trials), and the way they launch their products. One of the three drivers of the Commission's new industrial strategy is strengthening the single market to improve the EU's competitiveness in the world.

The SPC is well adapted to support innovation related to major technical developments that have emerged since 1992, such as biotechnology techniques. However, it was not designed as an incentive for research models based on incremental innovation (e.g. repurposing of existing molecules to address new and challenging therapeutic areas), but instead its purpose is to encourage innovation in novel active ingredients. Nor is the SPC, at least in its current form, expected to encourage R&D in areas where there is a lack of commercial viability, in particular on medicines for orphan and paediatric conditions (major areas of unmet health needs). This is because the SPC, the same as patent protection and regulatory market protection, is an incentive prolonging a period of exclusivity of sales of a product. SPC is not available for medical devices per se, but it can protect the active ingredient incorporated in a medical device.

6.4 Coherence

The provisions of the SPC Regulations are coherent internally , and the CJEU recently refined its earlier case-law on those provisions, which had provoked the most references. The SPC Regulations are also coherent with the future unitary patent system, and with regulatory legislation on pharmaceuticals and PPPs, even though some unclarity might remain over the

latter as to whether SPCs can be granted on the basis of certain categories of marketing authorisations. The evaluation of orphan and paediatric rewards[121] finds that because the SPC paediatric extension reward is granted nationally, it makes it difficult for companies to predict whether they will be granted an SPC extension.

The Bolar exemption applies to patents and SPCs for pharmaceutical products and provides a key legal framework for investment in development of generics and biosimilars in the EU. Most EU Member States provide for a Bolar exemption that is broader than the acts explicitly exempted in EU pharmaceutical legislation (and that will apply to unitary patents under the Unified Patent Court Agreement). This broader implementation, in some EU Member States, is preferred by the stakeholders consulted .

6.5 EU added value

The SPC legislative action taken at EU level creates added value through the incentives it provides to innovation in the fields concerned. This is largely confirmed by the stakeholders consulted. The alternative of purely national SPC legislations of EU Member States would have inherently suffered from various discrepancies, with a negative impact on the integrity of the EU's single market.

Medicines and PPPs are developed and marketed along global value chains, with stakeholders (including patients, who suffer from the same medical conditions and need the same treatments, subject to the same quality and safety requirements) that favour uniform, EU-wide regulatory and IP legal frameworks. Further, the EU is committed to establishing and ensuring the functioning of the single market with free movement of medicinal products and PPPs.

[121] SWD(2020) 163 final.

ANNEX 1: PROCEDURAL INFORMATION

1. Lead DG, Decide Planning

Lead DG: DG GROW

Planning reference: PLAN/2020/7977

2. Organisation and timing

Following several studies (see Section 4.1 and Annex 3) the Commission published an inception impact assessment in February 2017 announcing possible legislative and non-legislative proposals, and that the Commission will conduct a back-to-back evaluation and impact assessment of all relevant provisions and options for modernising the SPC Regulations. An ad hoc inter-service steering group (ISSG) was created to follow the implementation of this Inception Impact Assessment and in particular the preparation of this evaluation.

In October 2017, the Commission launched a 12-week online public consultation on the SPC system (see annex 2).

On 11 June 2019, the OJ of the EU published Regulation (EU) 2019/933 of the European Parliament and of the Council of 20 May 2019 amending Regulation (EC) No 469/2009 concerning the supplementary protection certificate for medicinal products. This regulation introduced the "SPC manufacturing waiver" one of the key elements of the inception impact assessment above.

This evaluation on the SPC system was launched in June 2019 after the adoption of Regulation (EU) 2019/933 on the SPC manufacturing waiver (which was a Commission priority in 2018 and 2019).

On 16 December 2019, the SPC ISSG was convened to discuss the detailed planning of the evaluation exercise. A second ISSG meeting took place on 11 May 2020, to discuss the first draft of the evaluation. Draft versions of this evaluation report were regularly shared with the ISSG, inviting comments and changes.

An interservice consultation was launched in August 2020.

3. Exceptions to the *Better Regulation* guidelines

No exceptions to the Better Regulation Guidelines

4. Consultation of the RSB (if applicable)

N/A

5. Evidence, sources and quality

This evaluation was based on the intervention logic of Regulations (EC) No 469/2009 and No 1610/96 and a comprehensive analytical framework comprising the evaluation questions and their respective judgement criteria, indicators and information sources.

As detailed in section 4.1 of this report, the data collection tools used to gather the relevant information consisted of a document review, stakeholder interviews, Commission public consultation, targeted survey, case studies, workshop, contracted and in-house studies.

ANNEX 2: STAKEHOLDER CONSULTATIONS

Several surveys and consultations by the Commission and contracted third parties were conducted, as well as a general public consultation. A summary of the main outcomes of these consultations/surveys are indicated below.

- *Commission public consultation*

An online public consultation on the SPC system and the EU Bolar exemption was conducted from 12 October 2017 to 4 January 2018.

The outcomes of that consultation are summarised in the document SWD(2018) 242[122].

Its main findings directly related to the current SPC regime (i.e. other than those concerning for instance targeted issues such as a possible unitary SPC or SPC manufacturing waiver) are as follows:

- Innovative companies' investment decisions (e.g. regarding R&D location) may be influenced by the existence and features of the SPC regime, but are essentially driven by a combination of many factors including e.g. access to a highly skilled labour force and a well-developed health infrastructure.
- Respondents broadly support the way in which SPC issues are regulated at Union level, which is considered globally effective. However, most of them report diverging practices for registration and SPC enforcement across Member States, i.e. a fragmented application of the SPC regime.

Comprehensive information on this public consultation can be found at: https://ec.europa.eu/info/consultations/public-consultation-supplementary-protection-certificates-spcs-and-patent-research-exemptions_en.

- *Allensbach surveys*

Two detailed surveys (the so-called Allensbach surveys) were conducted in the context of the MPI study mentioned below. One survey was addressed to patent offices and IP practitioners (including judges) and another one was address to the pharmaceutical industry. The outcomes can be found at https://ec.europa.eu/docsroom/documents/29524/attachments/4/translations/en/renditions/native.

Its main findings directly related to the current SPC regime (i.e. other than those concerning for instance targeted issues such as a possible unitary SPC or SPC manufacturing waiver) are as follows:

- 80% of the respondents consider that the current SPC regime fosters the investment in research and development (R&D) activities;
- 68% of the respondents consider that the current SPC Regulations act as an incentive to develop more products for which a longer time is needed until the marketing authorisation is obtained;
- 62% of the respondents consider that, when it comes to examining SPC applications, the practice and procedures of the national offices in the EU Member States differ significantly in terms of predictability, transparency and quality of the rights granted.

[122] https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1593699690365&uri=CELEX:52018SC0242

- *Inception impact assessment on the SPC and Bolar exemption*

No feedback[123] was received regarding the inception impact assessment of 2017.

- *Commission's survey on SPC transparency*

The Euroepan Commission launched a survey among national patent offices in early 2020 to obtain details on their transparency practices. Based on this survey, different practices across NPOs have been identified:

- Most national patent offices (NPOs) provide for an online searchable database, although the search criteria are very variable (in two MSs, only the SPC number can be used as a search criterion).
- Publishing SPC-related information takes varying amounts of time, ranging from a few days to several months, and even more than a year in specific situations.
- Only a slight majority of NPOs (14) publish SPC-related information in English in addition to their official languages.
- Only about half of the NPOs make the documents of the file of a given SPC application accessible online (e.g. in PDF format). However, the other ones usually provide for file inspection and/or are able to provide copies.
- Only a slight majority of NPOs (15) provide the European Patent Office with detailed information on SPCs (which the EPO then publishes).
- When asked which source they would consider to be the most suitable for providing centralised access to SPC information, 7 NPOs mentioned the EPO databases (possibly with improvements), 4 did not express any preference, and 14 mentioned a new centralised website.

[123] https://ec.europa.eu/smart-regulation/roadmaps/index_en.htm

ANNEX 3: METHODS AND ANALYTICAL MODELS

The evaluation is based on a number of studies (see detailed list below) and consultations/surveys (detailed in Annex 2).

The table represents the evaluation matrix of this report.

Objectives	**Judgement criteria and indicators**	**Data sources**
Objective 1 (more R&D on active ingredients)	- Global evolution of investments in pharma and PPP R&D - Evolution of approvals of new active ingredients at global and EU level	Mostly: OECD, US FDA and EMA data; Commission and MPI consultations; CE, Kyle and Mejer studies of 2017, EFPIA and Phillips McDougall consultants. Additional literature is mentioned throughout the corresponding sections.
Objective 2 (more R&D in the EU/prevention of delocalisation)	- Evolution of pharma and PPPs R&D investment and jobs in the EU	
Objective 3 (EU harmonisation)	- Registration and maintenance cost of the SPC, degree of procedural complexity, conflicting grant decisions, pending SPC applications across EU Member States, transparency/publication practices	Commission and MPI consultations, Alice de Pastors, CE, Kyle and Mejer studies of 2017. Additional literature is mentioned throughout the corresponding sections.

The following studies, which analyse and discuss economic and legal aspects of the SPC system, have been taken into account for this evaluation (it is not an exhaustive list).

a) Studies contracted or conducted by the European Commission

- A study contracted by DG GROW[124] to Charles River Associates on 'Assessing the economic impacts of changing exemption provisions during patent and SPC protection in Europe' (CRA study (2016));
- A study 'The economic impact of the Paediatric Regulation, including its rewards and incentives' (December 2016) contracted to Technopolis by DG SANTE[125], including an analysis of the paediatric SPC extensions.

[124] Directorate General for the Internal Market, Industry, Entrepreneurship and SMEs (DG GROW).

[125] Directorate General for Health and Food Safety (DG SANTE).

- An in-house DG GROW analysis of the SPC framework in the EU: '25 years of SPC protection for medicinal products in Europe: Insights and challenges' (Mejer study (2017));
- A study on the economic aspects of the SPC: 'Economic Analysis of Supplementary Protection Certificates in Europe' (Kyle study (2017)) contracted by DG GROW;
- A study on the legal aspects of the SPC conducted by the MPI study (2018)) contracted by DG GROW;
- A study analysing the combined effect of pharmaceutical incentives in Europe, realised by Copenhagen Economics (CE study (2018)) contracted by DG GROW and DG SANTE;

b) Studies/research conducted by various stakeholders (additional studies were consulted during desk research)

- R&D trends for chemical crop protection products and the position of the European Market, Phillips McDougall for ECPA, September 2013.
- De Pastors, A. "Latest News on Medicinal Product SPCs in Europe", 29 November 2015.
- V-Cumaran Arunasalam, Filip De Corte, Supplementary protection certificates for plant protection products: the story of 'The Ugly Duckling', Journal of Intellectual Property Law & Practice, Volume 11, Issue 11, November 2016
- Effects of supplementary protection mechanisms for pharmaceutical products, Technopolis Group, May 2018 (Technopolis study (2018))
- Evolution of the Crop Protection Industry since 1960, Phillips McDougall, November 2018.
- Batista et al., "IP-Based Incentives Against Antimicrobial Crisis: A European Perspective", published online, 16 January 2019, IIC (2019) 50:30–76.
- Kyle, M.K. The Single Market in Pharmaceuticals. Rev Ind Organ 55, 111–135 (2019). https://doi.org/10.1007/s11151-019-09694-6
- PricewaterhouseCoopers (PwC) study for EFPIA on the economic and societal footprint of the pharmaceutical industry in Europe, June 2019
- Biotech in Europe, Scaling Innovation, McKinsey, August 2019
- Hu, Y., Eynikel, D., Boulet, P. et al. Supplementary protection certificates and their impact on access to medicines in Europe: case studies of sofosbuvir, trastuzumab and imatinib. J of Pharm Policy and Pract 13, 1 (2020).

ANNEX 4: COSTS AND BENEFITS ANALYSIS OF PROLONGED EXCLUSIVITY DUE TO SPC

This annex provides qualitative and quantitative analyses of the costs and benefits of the SPC for medicinal products across different stakeholders. In this regard, the analyses below does not take the SPC in an isolated fashion, as its period of protection frequently runs in parallel with additional pharmaceutical-specific incentives such as the regulatory market protection.

This annex starts by analysing the additional sales obtained by the SCP protection and the cost associated, on the one hand, with developing and launching a medicine, and on the other hand, with maintaining and enforcing the SPC. The results of that initial analysis of sales and costs are used to calculate the costs and benefits of the SPC for distinct stakeholders (see summary in table 4.5 below). Table 4.6 depicts costs due to fragmentation and suboptimal transparency based on analysis of literature and consultations to stakeholders.

SPC holders' sales and cost of developing and launching a medicine

The SPC for medicinal products has a potential to stimulate new research if additional sales during the SPC help to recover R&D investments needed to develop and protect new therapies. At the same time, as also analysed further down, those additional sales have an impact on the public healthcare budgets of the EU Member States and on accessibility for patients.

4.1. Data

The analysis below relies on the Alice de Pastors database to identify medicinal products based on active pharmaceutical ingredients (APIs) which are SPC-protected. The analysis focuses on APIs for which their SPC application refers to centralised marketing authorizations granted between 1996 and 2014. It has been cross-checked with the data from the European Medicines Agency (EMA) and products withdrawn from the market has not been taken into account. Furthermore, SPCs that were refused or withdrawn were disregarded, and the sample is limited to those medicines for which an SPC application was filed in at least five EU Member States. The analysis then merges this data with the IQVIA Midas data linking API information. IQVIA Midas data (MAT/Q3/2019) reports information on the quarterly value and volume of sales from Q1 2008 to Q3 2019. It covers all members of European Union as of 2018, excluding Denmark, Cyprus and Malta, i.e. EU25 Member States.

The final sample covers information on 232 APIs to which an SPC was applied for and their sales information in the EU25. We further aggretate quarterly sales to annual series and focus on sales in years from 2008 to 2018.

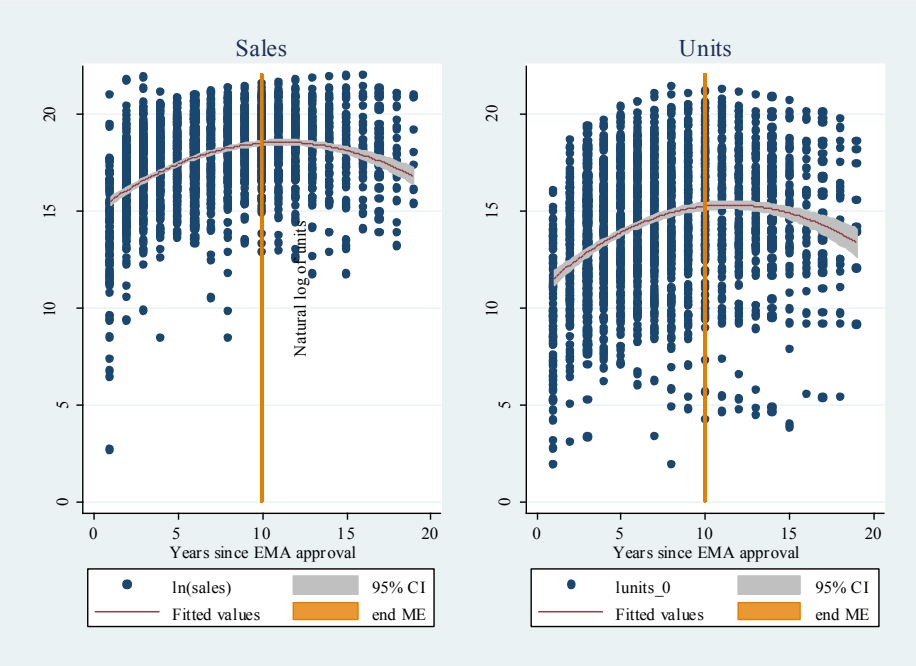
4.2. Sales: Impact of the SPC on the sales of the protected medicine

According to Kyle (2017) the average duration of effective protection term is **12.5 years**,[126] i.e. 9 for a basic patent protection and 3,5 for SPC. The impact of the SPC Regulation, however, has to be analysed along with other pharmaceutical incentives (see CE study (2018)). Innovative medicines benefit from regulatory market protection (see Annex 10) that is granted for 10 years and in some cases 11 years starting from their marketing authorization date. This reduces the effective time of SPC to 2.5 years.

[126] These numbers do not match the formula (article 13 of Regulation 469/2009) used to calculate the duration of SPC. This is because in the formula the SPC duration cannot exceed 5 years.

In order to estimate the impact of SPCs it is needed first to understand market sales dynamics. For 232 APIs in the sample,[127] figure 4.1 below shows the evolution of natural log of total originators' sales in EU25. Uptake of new medicinal product (volume units) is gradual and reaches its peak 8-10 years after the launch. The same holds for sales. This pattern is in line with previous findings in the literature.[128] The sales and uptake pattern reflect both sequential launches in UN Member States (MS) as well as increased uptake within a given MS.

Figure 4.1. Evolution of total sales and units in EU25, by number of years since EMA marketing authorization (natural log, constant prices 2018)



Note(s): Figure plots the natural log of total value of sales (left panel) and volume units (right panel) in the EU25 by number of years since EMA marketing authorization. Sales and units are those of innovator (marketing authorization holder) only. Vertical orange line indicates the end of market exclusivity period.

In order to measure the impact of the SPC on sales, the analysis below proceeds first to approximate the level of sales growth with the difference of natural logs and estimate the following regression:

$$\ln(sales_{iy}) - \ln(sales_{iy-1}) = \sum_{y=1}^{Y=15} \beta_y d_y + \gamma_t + m_i \qquad (4.1)$$

[127] APIs with marketing authorization granted before 2000 are excluded in order to cover at least five executive years of sales under IP protection.

[128] See for example Figure 4 in Lichtenberg, F. R. (2019). How many life-years have new drugs saved? A three-way fixed-effects analysis of 66 diseases in 27 countries, 2000–2013. *International Health*, *11*(5), 403-416.

where $sales_{iy}$ is a value of sales for API i in sale year $y \in [1,15]$ calculated from the year of EMA marketing authorization and d_y is a dummy variable indicating a year of sale, γ_t and m_i are calendar year and API fixed effects.

Table 4.1 shows estimated annual sales growth rate since the grant of EMA marketing authorization. In the first six years, the annual growth of sales is above 10%. After the sixth year, the growth slows down and comes to a halt in the tenth year that marks the end of regulatory market exclusivity.

SPCs can extend market protection beyond the regulatory market exclusivity of 10 years. Using estimated growth rates it is calculated the level annual sales by setting the level of sales in the second year equal to 100 monetary units (see column 3 in Table 4.1). Cumulative level of sales are shown in column 4. During the first ten years the total level of sales amount to 2 804 monetary units. For the additional 2.5 years, it is calculated the level of sales that could have been attained *with* and *without SPC protection*, i.e. under the generic competition. It is assumed that the level of annual sales during the SPC is the same as in the last year of market exclusivity period i.e. 396, which with SPC protection this yields to 25 * 396 = 990. Total sales then equal to 3 794. In this case, the total sales during SPC protection account for 26% of total sales *with SPC protection*. It is further assumed that loss of exclusivity leads prices to a drop of 50%.[129] Thus the level of sales during 2.5 years without SPC equals 990 * 0.5 = 445 and the total sales *without SPC* to 3 299. Thus it can be concluded that the SPC protection adds 13% to the turnover when compared to scenario *without* SPC protection.

Table 4.1. Evolution of sales during the regulatory market protection (with reference to year 2)

Years since EMA authorisation	Estimated Annual Growth Rate	Annual Sales	Cumulative Sales (monetary units)
2		**100**	**100**
3	92%	192	292
4	40%	267	559
5	23%	329	888
6	10%	362	1 250
7	5%	379	1 629
8	2%	385	2 014
9	3%	395	2 409
10	0%	**396**	**2 804**

Notes: DG GROW Chief Economist Team (CET)'s calculations. Annual growth rates for sale years 2-10 are estimated using regression (4.1). The level of annual sales is approximated by putting a value of 100 for sales in second year.

[129] Copenhagen Economics (2018) Study on the economic impact of SPC pharmaceutical incentives and rewards in Europe

4.3. Costs of developing and selling a medicine for the SPC holder

This section is focused on the costs and distinguishes three cost categories: cost of medicine development, cost of protection and cost of producing and selling goods. Additional costs, not taken into account, such as linked to regulatory pharmacovigilance apply.

4.3.1. Cost of development of a medicine

On the cost site, recent estimates by Wouters et al. show that the average capitalised research and development investment to bring a new medicine to market is EUR 1 122 million (95% CI: EUR 876 million – EUR 1 376 million).[130] DiMassi et al.[131] obtain average estimates in a similar range. Deloitte (2020)[132] shows that the average cost increased from EUR 917 m in 2009 up to EUR 1 656 million in 2019.

Based on these findings, it is assumed two values for medicine development costs: EUR 1 000 million (low) and EUR 1 600 million (high). Furthermore, as in the recent evaluation of orphan and paediatric legislation,[133] it is assumed that sales in the EU and USA cover medicine development cost and that the share of medicine development cost to be recuperated in Europe is 60%.[134] This leaves us a cost value between EUR 600 million (low) and EUR 960 million (high) to be covered with European sales.

4.3.2. Cost of protection

The cost of patent protection in EU27 countries amounts to EUR 152 765 and for SPC protection EUR 137 610 (both excluding agent fees).[135] In case of litigation, right holders need to account for EUR 50 000 - 250 000 cost per case per single jurisdiction.[136] This results in approximately EUR 500 000 spent on patent and SPC protection excluding agent fees. This cost is relatively small (0,08%) when compared to the low range estimate cost of EUR 600 million overall for bringing a new medicine to the market. Still this can be a prohibitive cost for SMEs or universities.

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130 Wouters, O. J., McKee, M., & Luyten, J. (2020). Estimated research and development investment needed to bring a new medicine to market, 2009-2018. *Jama*, 323(9), 844-853.

131 DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: new estimates of R&D costs. *Journal of health economics*, *47*, 20-33.

132 Deloitte (2019) Ten years on. Measuring the return from pharmaceutical innovation. Retrieved from https://www2.deloitte.com/us/en/pages/life-sciences-and-health-care/articles/measuring-return-from-pharmaceutical-innovation.html.

133 Joint evaluation of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products. SWD(2020) 164 final https://ec.europa.eu/health/human-use/paediatric-medicines/evaluation_en

134 This share could go further down if one considers growing sales in Asia.

135 The evaluation calculates the administrative cost of protection as EUR 4 745 (EP application, search and grant fees) + EUR 8 185 (EP renewal fees for 5-10) + 139 853 (renewal fees for 11-20 due at EU 27 national patent offices) = EUR 152 765. Validation and translation cost not included. Fee data comes from https://www.epo.org/law-practice/unitary/unitary-patent/cost.html. Annex 6 shows the levels of application and renewal fees for SPC protection. SPC application fee and renewal fees for up to four years for current EU27 are added.

136 Cremers, K., Ernicke, M., Gaessler, F., Harhoff, D., Helmers, C., McDonagh, L., & Van Zeebroeck, N. (2017). Patent litigation in Europe. *European Journal of Law and Economics*, 44(1), 1-44.

4.3.3. Cost of placing the medicine in the market

The analysis below focuses on EBITDA (Earnings Before Interest, Taxes, Depreciation, and Amortization). Research and development costs in EBITDA calculation are excluded, as in the cost-benefit analysis it is going to be evaluated whether the EBITDA (surplus in cash flow) suffices to cover drug development cost at product-level.

Since product-level accounting data is not available, the analysis proxys product costs using information on pharmaceutical company overall cost structure. EBITDA is calculated as gross profit - cash layout cost, i.e. cost of goods sold plus selling and administrative cost. For large pharmaceutical companies, cash layout cost represents 45% of profits[137] and it is assumed that it does not change with generic/biosimilar entry. Still, with expected price decline of 50% it keeps generic business of big pharma still profitable.[138] This is further demonstrated by the fact that, in addition to developing and marketing new treatments, many of innovating pharmaceutical companies own generic subsidiaries, and develop biosimilar products in addition to small molecules (see Kyle study(2017)).

4.3.4. Cost and sales balance

Using information on sales and costs as discussed above, it is calculated how many medicinal products breaks even during 12.5 years *with* and *without SPC* protection. Break-even means that research and development costs (as in 4.3.1) and cost of protection (as in 4.3.2) are covered with EBITDA (as in 4.3.3):

$$R\&D + IP\ protection \leq EBITDA$$

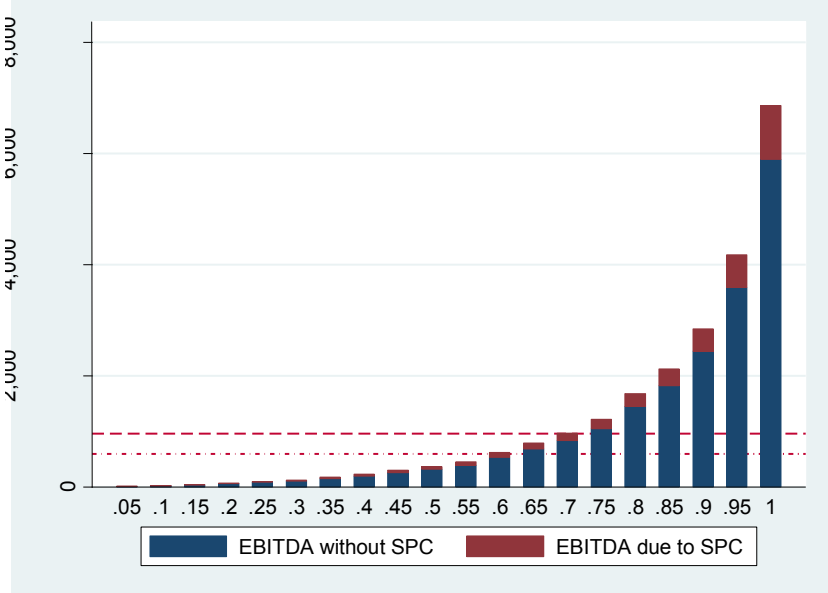
For 232 APIs in the analised sample, Figure 4.2 shows the distribution of EBTIDA. The distribution is skewed, dovetailing the fact that financial returns to pharmaceutical R&D are skewed in general.[139] Companies file SPC protection for a range of products with different profitability, plausibly, for each product that falls within the scope of SPC protection (as discussed in Kyle study (2017)). As profit potential of the API increases, the value of an extra year of market exclusivity increases as well. It is observed EUR 55 million (constant prices 2018) for a median APIs in terms of profits, EUR 160 million for average API, EUR 740 million for quantile 95 and EUR 1 063 million for quantile 99.

[137] McKinsey & Company (January 2017). Rethinking pharma productivity. Retrieved from https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/rethinking-pharma-productivity.

[138] 5 pp, representing 10% of the remaining turnover after genericisation.

[139] It is also confirmed in: J. W. Scannell, S. Hindsc and R. Evansc (2015) Financial Returns on R&D: Looking Back at History, Looking Forward to Adaptive Licensing, *Reviews on Recent Clinical Trials*, 2015, 10, 28-43.

Figure 4.2. Distribution of EBITDA and R&D costs (Source: DG GROW CET calculations)



For two levels of medicine development cost, Table 4.2 shows the share of SPC protected APIs that breaks even *with* and *without SPC* protection. 12.5 years of effective protection allows 32% to 42% of SPC protected products to break even. *Without* SPC protection, the share of SPC protected medicines breaking even is about 4 percentage points lower when compared to situation with SPC protection. But if incentives were to work at the product-level and via patent and SPC protection only, 60% of APIs would have never been developed and brought to the market.

Yet other mechanisms are at work. First, there could be cross subsidisation whereby EBITDA generated by high profitable APIs helps to finance development of other (less profitable) APIs. Second, product-specific development cost can differ. Furthermore, there are orphan incentives that help to develop niche product. Finally, public subsidies for research and development lower drug development cost, helping to bring less profitable products to the market.

Table 4.2: Percentage of medical products that break even (Source: DG GROW CET calculations)

Level of medicine development expenditure	With SPC	Without SPC
(low)	42%	38%
(high)	32%	28%

As per the above calculations, SPC protection adds 13% to the turnover during the first 12.5 years after market launch in the EU when compared to scenario without SPC protection. For 232 APIs in the analised sample, this amounts to additional total cash flow of EUR 37 billion. This amount would suffice to cover the research and development costs of between 39 and 62 new treatments (assuming high and low R&D costs respectively). Yet, as profitability is skewed, half of this impact comes from the Top 10% of best-selling APIs.

4.3.5. Market contestability

So far, it is assumed that each of the innovative medicines sees the entry of generics/biosimilars at the end of its protection period. Yet, this may not be the case. Table 4.3 below replicates Table 13 in the *Study to support the evaluation of the EU orphan regulation* (Final Report July 2019).[140] It shows the number of medicines with generic entry as a function of the average turnover. For medicines with an average turnover below EUR 10 million only 13% see generic entry and 64% do so for sales over EUR 1 billion. This indicates that markets gets more contestable as turnover increases.

Table 4.3 Level of generic entry (average turnover 2008-2016 in European Economic Area)

	< EUR 10 m	EUR10-100m	EUR100m-1b	>EUR 1b	All
Non-orphan medicines	132	81	76	53	342
With generic entry	17	24	30	34	105
Share	13%	30%	39%	64%	31%

Note: This table replicates Table 13 from the Study to support the evaluation of the EU orphan regulation (Final Report July 2019).

As part of the analysis, it is checked whether this pattern holds for SPC-protected products. The sample is constrained to those medicines that lost exclusivity before 2018, which leaves the calculation based on a sample of 69 APIs: 22 biologics and 47 non-biologics. Since the analysis is at the EU25 level, for each API the analysis takes the median value (across countries) of protection expiry year reported in IQVIA Midas as an indication for EU25 protection expiry.

Table 4.4 reports the results on market contestability. Out of 69 medicines, 48 (70%) saw the entry of generics/biosimilars. Taking turnover in the last year of regulatory market exclusivity as an indication of profitability, it can be seen that the level of turnover is higher for APIs that saw the entry (mean = EUR 372 million, standard deviation= EUR 450 million) when compared to no entry (mean = EUR 120 m, standard deviation = EUR 210 m). This is in line with the findings presented in table 4.3 that pharmaceutical market gets more contestable as profits increase.

[140] https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/orphan-regulation_study_final-report_en.pdf

Table 4.4: Generic and biosimilar entry (Source: DG GROW CET calculations based on IQVIA Midas data)

	Not Biologic	Biologic	Total
No Entry	7	14	21
Entry	40	8	48
Total	47	22	69

Table 4.3 indicates that the entry rate of generics is higher for non-biologicals than for biologicals. In other words, markets for biologics are less contestable than markets for non-biologics. This is not surprising as entry barriers for biosimilar are much higher than that for generic drugs. The first difference comes from the drug development costs. Development costs of biosimilar products amount to a few hundreds of million EUR and are more than 10 times higher than development costs of generic products i.e. 5 to 10 million EUR. Furthermore, timing of market entry also differs and it takes 5 to 9 years to develop a biosimilar treatment compared to 6 months to 2 years for generics.[141] Finally yet importantly, public procurement regulations and switching costs may inhibit entry.[142]

The turnover for generic and biological medicines that saw market entry can be observed. Indeed, biosimilar enters into markets with higher turnover (mean = EUR 683 million, standard deviation = EUR 593 million) than generic (mean = EUR 310 million, SD = EUR 397 million).

Today, markets for biologics are less contestable than for generics. In the futre this situation may change as development cost may go down and regulations are adjusted to promote uptakes put forward in EU Pharmaceutical strategy.

4.4. Cost of the SPC for public authorities

The Regulation on SPCs for medicinal products generates two types of costs for the public authorities: (i) administrative costs of granting SPC titles and (ii) costs to healthcare budget due to monopoly pricing during the SPC protection period that would exceed any other protection (e.g. regulatory market exclusivity).

As explained in Section 5.2.2, National Patent Offices administer SPC and national courts deal with enforcement aspects. For large patent offices, SPC examination adds little work to patent examiners (see Annex 7 for details). Small offices, however, seem not to have sufficient administrative capacity to conduct substantive examination of the SPC applications.

As concerns impact on healthcare budgets, new medicinal products are in general more expensive. The cost to authorities and society of SPC protection is equal to the additional revenues pharmaceutical companies receive during the additional 2.5 years of SPC protection (if it is considered that regulatory market protection is only 10 years, and not 11 years).

[141] See Annex 4 in Impact Assessment Accompanying the document Proposal for a Regulation of the European Parliament and of the Council amending Regulation (EC) No 469/2009 concerning the supplementary protection certificate for medicinal products SWD(2018) 240 final.

[142] c.f. Morton, F. M. S., Stern, A. D., & Stern, S. (2018). The impact of the entry of biosimilars: Evidence from Europe. *Review of Industrial Organization*, 53(1), 173-210.

Governments are thus spending 13% more on SPC protected products when compared to situation without SPC.

4.5. Impact on patients

By generating new sources of revenues, SPCs contribute to the development of new medicinal products. Recent evidence shows that new medicine launches have reduced years of life lost (YLL) before three different ages (85, 70, and 55) from 34 up to 42%.[143] Furthermore, the introduction of a new cancer medicine in a country was associated with a decline in cancer mortality of 8% for men and 9% in women. Improved quality of life was also reported in respect of chronic diseases.[144]

The downside, however, could be that extended protection due to SPC protection delay patient access. Governments are the ultimate buyers of innovative pharmaceuticals. Given limited financial resources, they may not afford serving all patients in needs. Figure 4.1 shows that the uptake of new treatments reaches its peak 8 to10 years from the market launch, i.e. at the end of regulatory market exclusivity period.

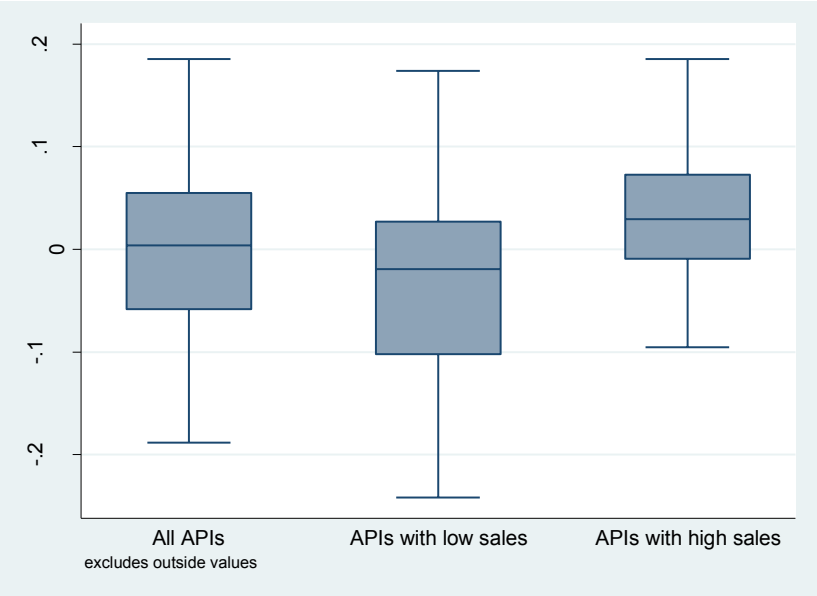
Taking 48 APIs in the analised sample for which there was a generic/biosimilar entry (see Section 4.4 in this Annex), it is analysed the volume growth rate of total units sold in the three years after entry. Total units sold equal units sold by innovator plus units sold by generic/biosimilar. The analsyis relies on standard units reported in IQVIA Midas data.

Figure 4.4 shows the results of our analyses. Median annual volume growth post-entry is slightly above 0.3%. This indicates that in half of cases the total volume is increasing and in the other half decreasing. The analysis further differentiates between APIs with high and low gross sales. As a cut-off point, the analysis takes average turnover in the last year of regulatory market exclusivity (EUR 233 m). For 23 APIs with high gross sales, the market volume keeps growing annually at an average rate of 3% after the generic/biosimilar entry. Calculations show that in these markets 7.5% more patients are treated during the period of 2.5 years after the entry when compared to the end of market regulatory exclusivity. This is not the case for the remaining 23 less profitable APIs.

[143] Lichtenberg, F. R. (2019). How many life-years have new drugs saved? A three-way fixed-effects analysis of 66 diseases in 27 countries, 2000–2013. *International Health*, *11*(5), 403-416.

[144] OECD Health Policy Studies (2018) Pharmaceutical Innovation and Access to Medicines.

Figure 4.3. Volume growth rates post entry by value of gross sales.



Notes: Figure plots annual growth rates for the first three years post entry. Total volumes represents the sum of innovators volumes and that of generic. The first bar includes all 48 APIs that saw generics or biosimilarsentry, the second (third) APIs with low (high) gross sales in the last year of regulatory market exclusivity. The cut-off point is given by EUR 233 million. The horizontal line in the box represents the median value for each group. The upper (bottom) hinge of the box indicates the value for 75th (25th) percentile.

Table 4.5: Summary of Cost Benefit Analysis

Stakeholders	Cost (in EUR)	Benefits (in EUR)	Result
Innovators (SPC users)	Patent & SPC Protection : Patent (EP): EUR 0.15 m SPC (4y): EUR 0.14 m Attorney: (NDA) Litigation (one case): EUR 0.05- 0.2 m SPC search & monitoring: (NDA)	SPC protection adds 13% to the turnover during the first 12.5 years after market launch of a medicine in the EU. For 232 APIs in the sample this amount to a total of EUR 37 051 m. The cash flow increases as market potential (turnover) increases: Median: EUR 55 m Average: EUR 160 m Top 5% selling medicines in our sample: EUR 740 m Top 1%: EUR 1 063 m	The profitability is skewed and half of this additional cash flow is due to the Top 10% of APIs of our sample (in terms of sales).
Generics/biosimilar	Litigation (one case): EUR 0.05- 0.2 m SPC search & monitoring: (NDA)	Introduction of new products creates new markets for generic and biosimilar products.	
Legal profession	Familiarisation with SPC rules and legal system, including cross-border	Litigation (cost per case): EUR 0.1- 0.5 m Attorney fees for managing patents and SPC applications: (NDA)	
Public Authorities and Society	*Patent offices* SPC application account for > 10% of the patent examination workload in small MS and < 1% in largest MS. *Public health budgets* SPC protection adds 13% to the total spending on SPC protected pharmaceuticals during the first 12.5 years after market launch in the EU.	The new medicine launches have reduced years of life lost (YLL) before three different ages (85, 70, and 55) from 34% up to 42%.Furthermore, the introduction of a new cancer medicine in a country was associated with a decline in cancer mortality of 8% for men and 9% for women.[145] Improved quality of life in respect of chronic diseases.[146] Treatment foregone seems to be is limited to high profitable APIs only. For 25 high profitable APIs that saw generics entry, 7.6% more patients could be treated during 2.5 years if there was *no SPC* protection.	Additional cash flow generated due to the SPC would suffice to cover the research and development costs of between 39 and 62 new treatments. Treatment foregone concerns high profitable APIs only.

Notes: See Annex 4 for details on the analysis of the impact on innovators (SPC holder) as well as calculations on treatment foregone. Additional sales due to SPC are in relation to counterfactual scenario of having no-SPC protection. See Annex 7 for the workload of national patent offices.

[145] Dubois, P., & Kyle, M. (2016). The Effects of Pharmaceutical Innovation on Cancer Mortality Rates.

[146] OECD Health Policy Studies (2018) Pharmaceutical Innovation and Access to Medicines.

Fragmentation & Transparency

Table 4.6: Main costs due to fragmentation and suboptimal transparency based on analysis of literature and consultations to stakeholders

Stakeholder	Qualitative assessment of cost
SPC holders (originators)	- Redundant granting procedures resulting in legal uncertainty and additional red tape, and administrative and legal counselling costs. - Redundant litigation and abundant national case law, increasing legal uncertainty, cost and red tape. - Difficult national monitoring of the use of the SPC manufacturing waiver by generics and biosimilars makers. - Uncertainty about obtention of the SPC paediatric extension. Those costs could be significant for SMEs, which count with less financial resources, reduced in-house specialists and limited multi-geographical presence. Licensing can be more complex to handle. Innovative SMEs play a significant role in the pharmaceutical sector (already in 2009 the Commission's pharmaceutical sector inquiry reported that approximately 25% of molecules in clinical development were acquired from other companies, including SMEs. More recently, EMA statistics show that 44% (15 out of 34) of priority-medicine applications granted in 2017 came from SMEs).
Companies dealing with generic products	- Expensive search and monitoring of SPCs in force/or expired in multiple EU Member States. - Monitoring difficulties are exacerbated in the absence of proper transparency (different publication practices across Member States). - Redundant and cross-border litigation and abundant national case law induce increasing legal uncertainty, cost and red tape. - Different Bolar scope across EU Member States. - Complex use of the SPC manufacturing waiver if cross-border activities (e.g. logistics and outsourcing of production) are necessary. Those challenges are especially negative for SMEs.
Consumers and patients, and health authorities	- Limit the availability of innovative medicines Uncertainty and high cost of filing patent and SPC applications in multiple EU Member States can lead SPC holders to neglect protection in less attractive EU Member States' markets and therefore to postpone launches of their innovative products in those markets. A unitary SPC could help overcome this issue. - Adverse impact on the accessibility to medicines Fragmentation and lack of transparency on the status and scope of SPC protection across EU Member States cause delays in the entry of generics in the EU, especially in less profitable EU Member States. - Could hamper joint public procurement initiatives by a group of EU Member States (e.g. where the SPC scope or duration is not the same in all of these Member States).

National patent offices and national courts	- The increasing complexity of the state-of-the-art and the lack of transparency make it more difficult for national patent offices and national courts with fewer resources to deal with examination of SPCs.

ANNEX 5: EVOLUTION OF THE APPROVAL OF NEW ACTIVE INGREDIENTS

Taking the annual approvals of "novel drugs"[147] by the Center for Drug Evaluation and Research of the US Federal Drug Administration as a proxy[148] for the generation of "new active ingredients" at world level, it can be observed the following in the figures 5.1 and 5.2 below[149,150]:

- **From 1975 to 1994**: a moderate positive trend in the approvals of novel medicines, from 15 approved in 1975 up to around 20 in 1994 with a peak of 30 in 1991.

  Within this period, in 1984, the USA introduced the patent term extensions (the US version of the EU's SPCs) along with other measures[151] through the US Medicine Price Competition and Patent Restoration Act (Hatch-Waxman Act). South Korea and Japan introduced patent term extensions in 1987 and 1988 respectively.

- **From 1994 to 1999:** a surge in the approvals of novel medicines is observed, from around 20 in 1994 to over 50 in 1999.

  Given the timing necessary to develop a new medicine, the measures introduced in the US, Japan and South Korea in the previous decade (described above) likely contributed to the highly positive results in term of new medicines approvals seen in this decade. In addition, it was at the beginning of this decade that the Commission proposed legislation to introduce the SPC in the EU.

  Further, this spike in the approvals in late 90s has to be seen in the context of the adoption of the Prescription Drug User Fee Act (PDUFA) in 1992.[152] PDUFA introduced measures for the FDA to eliminate the backlog of un-reviewed applications within 24 months of the establishment of an user fee program. In 2002, the US Government Accountability Office reported that PDUFA funds allowed the FDA to increase the number of new drug reviewers by 77% in the first eight years of the act.

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147 According to the annual reporting documentation of the Center for Drug Evaluation and Research of US Federal Drug Administration (FDA), "novel drugs" are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient treatments. The active ingredient or ingredients in a novel drug have never before been approved in the United States. These "novel drugs" are approved either as new molecular entities (NMEs) under New Drug Applications (NDAs), or as new therapeutic biologics under Biologics License Applications (BLAs)). In some cases an NME may have actions similar to earlier drugs and may not necessarily offer unique clinical advantages over existing therapies. (https://www.fda.gov/media/134493/download).

148 The use of this proxy can be found in several studies. See pages 203 and 219 of CE study. Registrations in the EU can be done through decentralised procedures involving the national medicine agencies of EU Member States, and the centralised procedure with the scientific assessment of the European Medicines Agency.

149 Munos B. (2009), Lessons from 60 years of pharmaceutical innovation. *Nature Reviews Drug Discovery*, *8*(12), 959.

150 https://www.nature.com/articles/s41587-019-0021-6

151 e.g. a 5-year period of data exclusivity, and the establishment of the Orange Book where the US FDA publishes the patents which originators believe cover their approved medicines.

152 Mary K. Olson, PDUFA and Initial U.S. Drug Launches, 15 Mich. Telecomm. Tech. L. Rev. 393 (2009).

- **From 1999 to 2010 (Figures 5.1 and 5.2 below):** a significant decline of approvals of novel medicines back to the levels of 1994.

  In 2008 the European Commission launched a pharmaceutical sector inquiry that concerned, inter alia, obstacles for innovative products, i.e. obstacles to competition between originator companies.

- **From 2010 to 2019 (Figure 5.2):** a new surge in approvals to a historic record of 59 new novel medicines, including 20 biologics, in 2018. Year 2019 concluded with a strong output of 48 novel medicine approvals, with 21 of them (44%) approved to treat orphan diseases. Medicines with orphan indications enjoy specific incentives under provided by the Orphan Regulation.

Specifically for **biologicals**, the figures below show a positive trend on the generation of new active ingredients since the emergence of biotechnology in the 1980s.

Figure 5.1: US FDA approvals of new molecular entities (1950 – 2008) (Source: FDA databases)

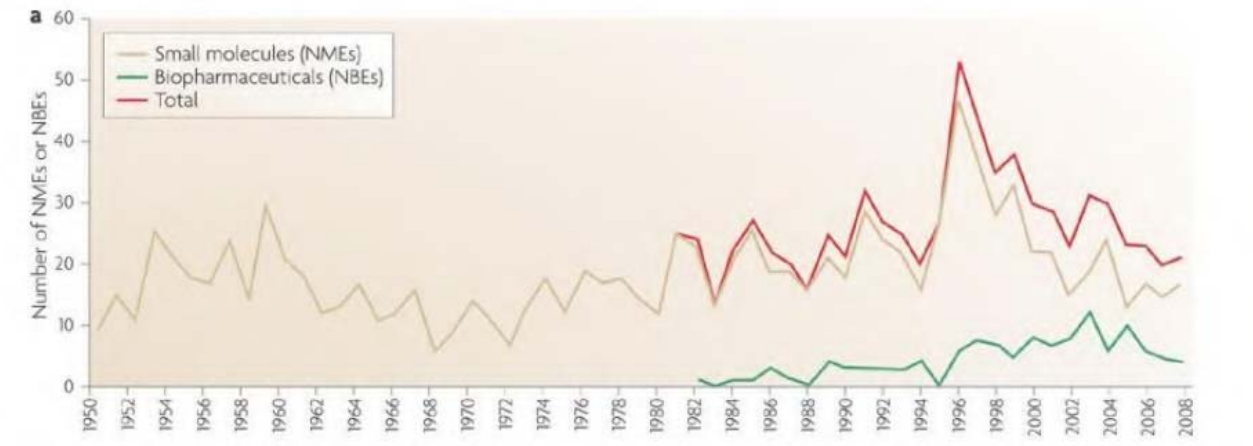
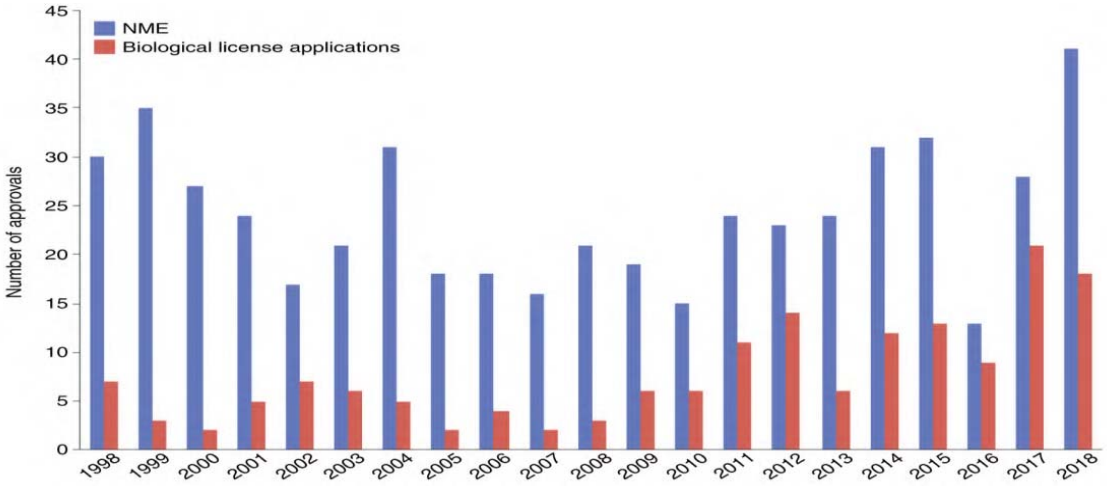


Figure 5.2: US FDA approvals of new molecular entities (1988 – 2018) (Source: FDA databases)



ANNEX 6: LEVEL OF SPC APPLICATION AND RENEWAL FEES

Level of SPC application and renewal fees as of April 2016 (in EUR)

	Application Fees	SPC Renewal fees				
		1st year	2nd year	3rd year	4th year	5th year
AT	363	2,611	3,029	3,448	3,864	4,282
BE	200	650	700	750	800	850
BG	256	1,023	1,278	1,534	1,790	2,045
CY	100	700	740	780	820	860
CZ	185	962	1,036	1,110	1,184	1,258
DE	300	2,650	2,940	3,290	3,650	4,120
DK	403	685	685	685	685	685
EE	105	630	630	630	630	630
ES	496	812	853	896	942	991
FI	450	900	900	900	900	900
FR	520	940	940	940	940	940
UK	305	732	854	976	1,098	1,220
EL	250	1,200	1,300	1,400	1,500	1,800
HR	398	1,593	1,991	2,389	2,788	3,186
HU	756	943	1,130	1,321	1,508	1,695
IE	95	468	468	468	468	468
IT	404	1,011	1,011	1,011	1,011	1,011
LT	115	347	347	347	347	347
LU	50	410	420	430	440	450
LV	120	550	550	550	550	550
MT	116	245	256	268	280	291
NL	544	1,600	1,800	2,000	2,200	2,400
PL	126	1,375	1,375	1,375	1,375	1,375
PT	418	731	784	836	888	941
RO	500	1,000	1,100	1,200	1,300	1,400
SE	528	1,056	1,056	1,056	1,056	1,056
SI	420	1,702	2,102	2,504	3,004	3,404
SK	166	996	1,328	1,660	1,992	2,324
Min	50	245	256	268	280	291
Max	756	2,650	3,029	3,448	3,864	4,282
Average	310	1,019	1,129	1,241	1,357	1,481
Total EU27	8,384	27,789	30,749	33,777	36,911	40,259
Total EU28	8,689	28,521	31,603	34,754	38,009	41,479

Source: National patent offices' websites.

ANNEX 7: SPC WORKLOAD AT NATIONAL PATENT OFFICES

SPC workload at national patent offices

	1995		2000		2005		2010		2015		2018	
	(A)	(B)	(A)	(B)	(A)	(B)	(A)	(B)	(A)	(B)	(A)	(B)
AT	7	0.3%	31	1.3%	40	1.6%	43	1.6%	38	1.5%	50	2.2%
BE	5	0.5%	28	3.3%	39	5.9%	38	4.8%	40	3.5%	46	4.0%
BG							9	3.3%	24	7.6%	43	17.8%
CY					11	14.7%	19	70.4%	8	53.3%	33	89.2%
CZ					18	2.1%	18	1.8%	27	2.8%	52	6.6%
DE	16	0.0%	30	0.0%	47	0.1%	41	0.1%	45	0.1%	65	0.1%
DK	8	0.5%	21	1.1%	50	2.7%	35	1.9%	40	2.3%	41	2.7%
EE					6	13.6%	7	6.7%	29	44.6%	34	53.1%
ES			29	0.9%	43	1.3%	38	1.0%	38	1.2%	61	3.5%
FI	8	0.2%	14	0.5%	28	1.3%	33	1.8%	37	2.5%	42	2.7%
FR	30	0.2%	29	0.2%	44	0.3%	47	0.3%	46	0.3%	59	0.4%
GB	21	0.1%	28	0.1%	41	0.1%	48	0.2%	45	0.2%	46	0.2%
GR			30	8.1%	30	5.9%	33	4.2%	32	5.3%	52	8.2%
HR									20	9.7%	23	14.5%
HU					19	1.6%	15	2.1%	38	5.7%	47	9.6%
IE	8	2.2%	27	5.8%	31	7.1%	35	9.1%	41	16.8%	46	29.9%
IT	11	0.1%	24	0.3%	41	0.4%	41	0.4%	45	0.5%	63	0.6%
LT					8	6.5%	11	8.8%	28	19.0%	n.a.	
LU	8	7.1%	25	12.4%	40	31.3%	35	25.9%	26	9.5%	36	8.4%
LV					8	4.5%	12	6.1%	17	11.0%	32	22.5%
MT									3	21.4%	18	
NL	17	0.6%	30	1.0%	43	1.5%	39	1.4%	40	1.6%	n.a.	
PL					15	0.2%	16	0.5%	27	0.6%	58	1.3%
PT			19	11.5%	29	12.4%	36	6.2%	40	4.1%	53	7.1%
RO							15	1.0%	30	2.8%	45	3.8%
SE	18	0.4%	31	0.6%	37	1.2%	39	1.5%	40	1.6%	46	2.0%
SI					13	3.4%	15	3.2%	33		36	11.5%
SK					11	4.2%	17	5.7%	30	10.5%	41	15.1%

Note: Column (A) shows the number of SPC applications and column (B) the share of SPC application in the total patent workload i.e. number of patent applications (direct and PCT national phase entries) plus SPC applications.

Source: Numbers of SPC applications come from Alice de Pastors database for all selected years except 2018. For 2018 information comes from the EPO Document No. EPO CA/36/19 – 'Exchange on information on current trends in activity at the NPOs and at the EPO'. The numbers of patent applications (direct and PCT national phase entries) are from WIPO's IP Statistics Data Center.

ANNEX 8: THE QUESTIONS PER EACH OF THE FIVE EVALUATION CRITERIA

Questions related to the **effectiveness** criterion:

- Question 1: Has worldwide innovation in new active ingredients increased since the introduction of the SPC system?
- Question 2: Was the observed increase in investment in research on new active ingredients induced by the SPC system?
- Question 3: Have more pharmaceutical and PPP investments and jobs in R&D been brought to the EU since the introduction of the SPC? How have those investments developed in other trading partners of the EU?
- Question 4: To what extent did the SPC Regulations increase investments in pharmaceutical and PPP innovation in the EU?
- Question 5: Are the SPC grant, enforcement and publication procedures/outcomes uniform across the EU?

Questions related to the **efficiency** criterion:

- Question 6: What is the impact of the SPC on the availability, accessibility and affordability of medicines?
- Question 7: Is the maximum duration of the SPC appropriate ?
- Question 8: What are the costs to stakeholders of the fragmentation of the SPC system?

Questions related to the **relevance** criterion:

- Question 9: How well do the original objectives of the SPC Regulations still correspond to the needs within the EU (i.e. are the objectives of more innovation in new products, more innovation activities in the EU, prevention of delocalisation, and promotion of a homogenous SPC system in the EU still relevant)?
- Question 10: To what extent have the original objectives proven to have been appropriate for the SPC Regulations?
- Question 11: How well adapted are the SPC Regulations to new technological developments?
- Question 12: How well is the SPC Regulation adapted to public health crises, such as the COVID-19 pandemic, and how it can contribute to the EU recovery?

Questions related to the **coherence** criterion:

- Question 13: Are the SPC Regulations internally coherent in their respective provisions?
- Question 14: To what extent is the SPC framework externally coherent with EU legislation on regulatory pharmaceutical legislation, patent law, the unitary patent package and the Bolar exemption? Are there any gaps, overlaps or inconsistencies?
- Question 15: To what extent is the SPC coherent with other EU pharmaceutical and PPP-specific incentives for innovation?
- Question 16: To what extent are the SPC Regulations coherent with international law/obligations?

Question related to the **EU added value** criterion:

- Question 17: What is the additional value resulting from the SPC Regulations, compared to what would reasonably have been expected from Member States acting at national level?

ANNEX 9: SWOT TABLES: THE EU AS A LOCATION OF R&D INVESTMENT IN THE PHARMACEUTICAL AND PPPS SECTORS

The following SWOT (strengths/weaknesses/opportunities/threats) tables have been drawn using information extracted from the studies and consultations discussed in Section 5.1.2.

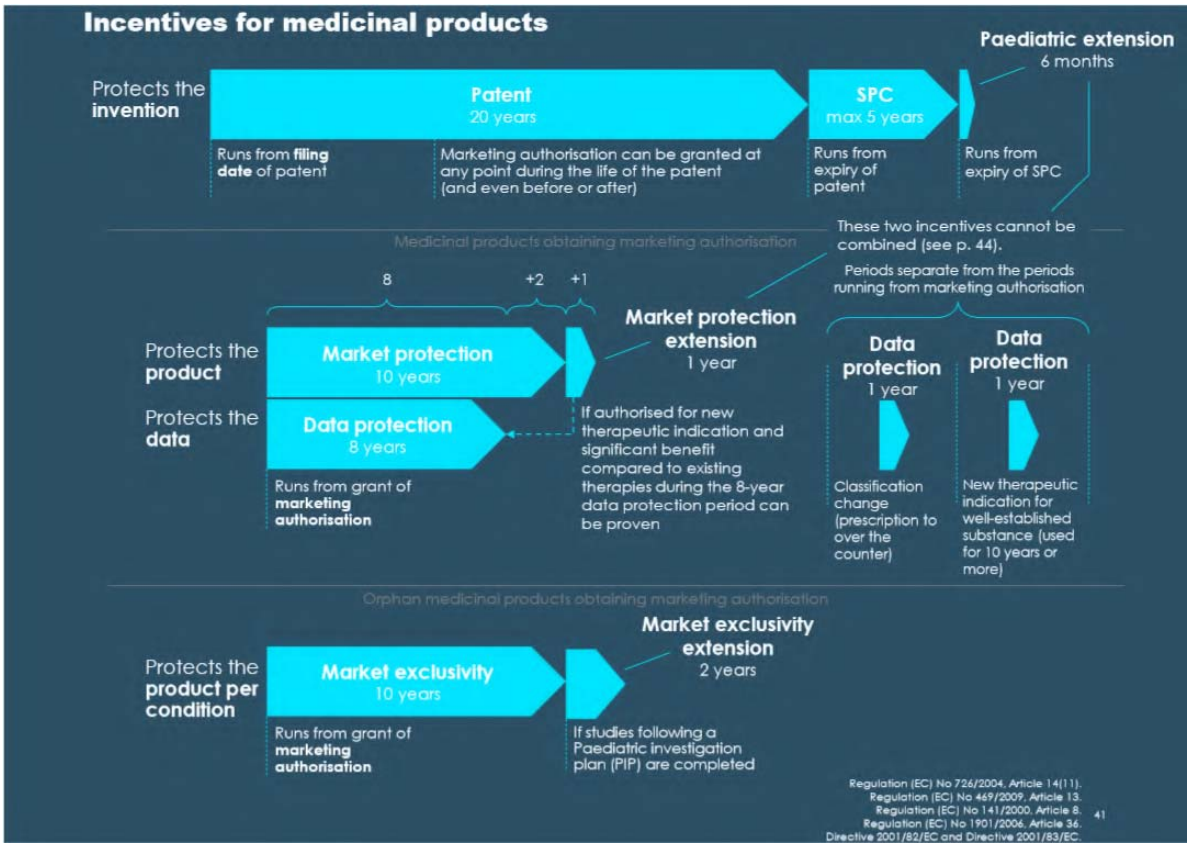
SWOT table: the EU as a location of R&D investment in the pharmaceutical sector	
Strengths	**Weaknesses**
- Strong IP. - High level of labour skills. - World class science. - Strong infrastructure. leading in number of trials. - 32% of the top 50 life science universities were based in EU in 2019. - EU is leader in publications.	- Increasing private financing gap versus the US one (pension funds, and venture capital), especially in late-stage. The average US initial public offering (IPO) is three times larger than on European markets. - Fragmentation of the Single Market for SPC. - Limitations of certain labour profiles for biotech and related start-ups (e.g. managers) and difficulties to attract/retain that missing talent. Higher risk-aversion comparing to the US. - Publications not always translated into patents (the USA and China perform better) and medicines (in biotech. in 2017-2018. the US biotech industry registered 6 times more medicines at the US FDA than EU biotech). The USA originates 70% of the publications with commercial potential.
Opportunities	**Threats**
- Internal market: potential size of capital markets, unitary patent/SPC, EU public funding (e.g. Horizon 2020), Commission start-up initiatives and European Scale-Up Action for Risk Capital (ESCALAR) to enable venture capital funds to increase their investment capacity. - Creation of a "European Biomedical Advanced Research and Development Authority". - The COVID-19 pandemic exposed the increasing dependency of the EU to imports of active pharmaceutical ingredients from Asia, especially for generics . - EU biotechs in 2018 were stronger than the US biotechs in "early innovation". - Increasing venture capital, especially for early stage venture rounds. - Promising biotech pipeline: European biotechs do better on emerging modalities, driving 32% of all phase 3s and registrations.	- China to overtake the EU as the 2nd largest pharma market. Korea and India are massively investing in the pharmaceutical industry. - US private funds purchase EU startups and delocalise their activities. - The UK's withdrawal from the EU after having built a critical mass with 35% of all new biotech in Europe. - Less trials in Europe (32%) on cell and gene therapy than the USA (50%).

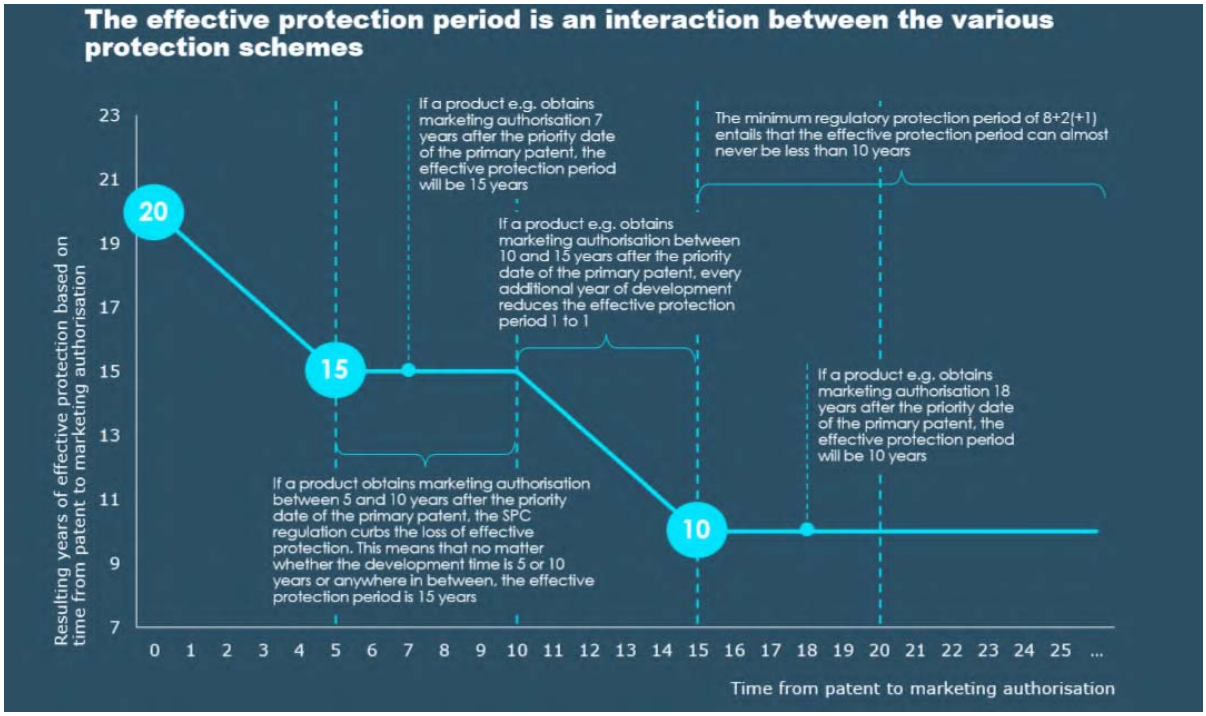
SWOT table: the EU as a location of R&D investment in the PPPs sector	
Strengths	**Weaknesses**
- Strong IP protection. - High level of labour skills and world class	- Strict regulatory environment. - Fragmentation of the Single Market for SPC.

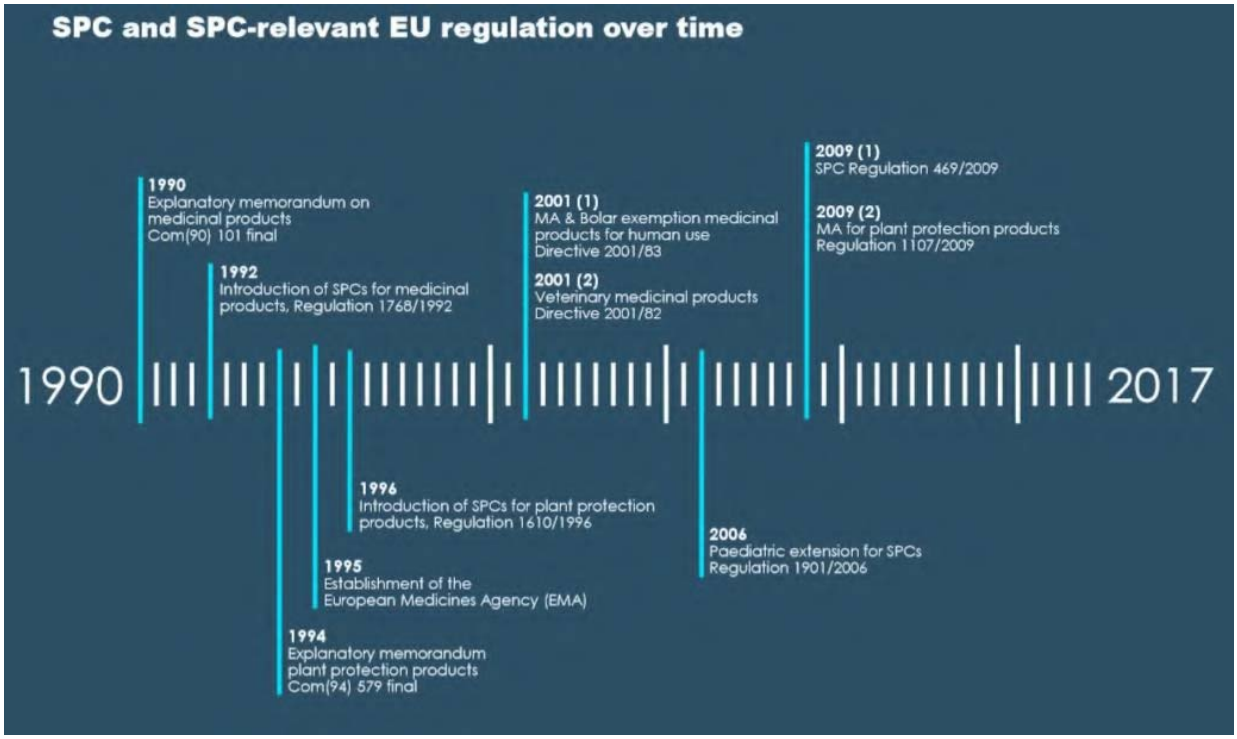
science. - Major PPP companies are headquartered in the EU. - Leading export output.	- Mature nature of EU-15 markets. - Harsh European regulatory environment.
Opportunities	**Threats**
- New R&D techniques. - Still growing market in the EU-12 and need for more added-value products in EU-12.	- Asia has overtaken Europe as the first market for PPPs in the world. Attraction of developing markets driven by volume growth. - Decline of the number of active ingredients developed for the European market. - Shift in investment to seeds & traits R&D for non-European markets. - Non-acceptance of genetically modified (GM) seeds in the EU while investment in agrochemical R&D is focusing in the GM seed sector.

ANNEX 10: PHARMACEUTICAL INCENTIVES IN THE EU

The graphics below are obtained from the CE study of 2018, which further explains them.






SPC and SPC-relevant EU regulation over time
1990
2017
1990
Explanatory memorandum on medicinal products Com(90) 101 final
1992
Introduction of SPCs for medicinal products, Regulation 1768/1992
1994
Explanatory memorandum plant protection products Com(94) 579 final
1995
Establishment of the European Medicines Agency (EMA)
1996
Introduction of SPCs for plant protection products, Regulation 1610/1996
2001 (1)
MA & Bolar exemption medicinal products for human use Directive 2001/83
2001 (2)
Veterinary medicinal products Directive 2001/82
2006
Paediatric extension for SPCs Regulation 1901/2006
2009 (1)
SPC Regulation 469/2009
2009 (2)
MA for plant protection products Regulation 1107/2009

ANNEX 11: EU INDUSTRIAL ECOSYSTEMS AND EU RECOVERY

The Commission Communication on A new industrial strategy for Europe (COM(2020) 102) states that "ecosystems encompass all players operating in a value chain: from the smallest start-ups to the largest companies, from academia to research, service providers to suppliers".

The Commission has currently identified 14 preliminary ecosystems, which selection and definition was done in the context of the preparatory work for the Recovery Plan Communication "Europe's moment: Repair and Prepare for the Next Generation". The figure below shows the list of ecosystems and their indicative composition.

The EU SPC system works directly with two of the ecosystems, Health and Agri-food.