Mapping the European Patent Landscape for Medical Uses of Known Products

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European Patent Office data shows an increasing number of patents for medical uses of known products.

Most countries active in pharmaceutical innovation provide some sort of patent protection for new medical uses of known products. This provides market exclusivity, for example, when investigators find a new, non-obvious medical indication for a drug previously patented as a new, non-obvious molecule. Yet, despite clear policy importance of developing new treatments quickly and cheaply, surprisingly little is known about the scale and impact of these patents.

Without more information, it is perilous for judges, policymakers and patent offices to presume they can propose or interpret rules on the validity and infringement of patents for new medical uses with reasonable chances of desirable social outcomes. How sought-after are new medical use patents? Is their popularity waxing or waning? Who is benefitting from this government-granted market protection? What types of claims are being used to protect these inventions? Is it true that serious disadvantages would follow if such patents were harder to obtain or to enforce? Should they be easier to obtain and enforce? Who will be the winners and losers if rules on acquisition and infringement are adjusted?

These issues are particularly important for the field of pharmaceutical research known as 'repurposing'. This field of research holds much potential, since it is often quicker and cheaper to develop a drug for a new use if it is already known to be tolerated by the human body. However, research still involves financial outlay and risk, for example, for phase II and III clinical trials, as well as EMA/FDA authorization. A current debate is whether policy offers sustainable business models for repurposing; sustainable not only for innovators but also healthcare purchasers seeking proportionate-pricing. This debate is taking place in both Europe and the US.[1,2] Another question is whether repurposing research is a field where smaller and more public-oriented organisations (e.g. SMEs, universities, governmental facilities and hospitals) could compete with larger pharmaceutical companies, ideally with consequent benefits for the public purse.[3]

Many commentators argue that the patent system is failing to provide suitable incentives for repurposing —new medical use patents are too hard to obtain and too hard to enforce when generic companies sell the off-patent drug molecule for off-patent uses.[4] Signs of failure would include declining rates of new use patent applications and low grant rates. Additionally, the identities of applicants of new use patents would shed light on the competitiveness of smaller and public organizations. But to date investigations have not looked for such evidence. This article takes steps to address the empirical gap using European Patent Office (EPO) data.

The EPO grants patents covering 38 Member States, including the UK. Studying the European landscape for new medical use patents is particularly fascinating and challenging because the relevant patent laws are particularly complex. Unlike the US, it is not possible to patent a new medical indication as a method of treatment due to the rule in Article 53 of the European Patent Convention 2000 ('EPC') which provides: 'patents shall not be granted in respect of methods for treatment of the human body …'. Side-stepping this restriction – which was not intended to apply to drug products or methods beyond treatment, surgery and diagnosis – EPC Member States grant patent exclusivity over 'uses' of products and (until January 2011) methods of manufacturing drugs for particular uses. However such claims must invoke special novelty saving provisions found in Art. 54(4) and 54(5) EPC, or be drafted as Swiss-

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type claims. Otherwise new medical use claims would be anticipated by the prior disclosure of the substance or composition (e.g., the known molecule). After all, the functional traits of the molecule have not changed; the molecule has been 'suitable for' all of its uses from the moment the molecule is publicly available even if human beings have not been consciously aware of the effects.

Another challenge is that to understand properly whether the patent system supports repurposing as a viable domain, the landscape has to distinguish patents (and patent families) that claim the molecule of interest with the same priority date as the new medical use of that molecule. Such patents are not examples where repurposing is perhaps under-incentivized; they reflect standard business models and legal practice following elucidation of a new molecule, composition or substance.

Another European intrigue is that Swiss-type claims are being phased out, following a transition period after the introduction of Art. 54(5) EPC. This decision affects patent applications with priority dates on or after 29 January 2011.[5] In theory then, all Swiss-type claim protection should expire at the latest on 29 January 2031. However, empirical research is necessary to identify the practical completion of Swiss-type claim protection. This carries more than academic interest in Europe. Lately questions about the validity and infringement of Swiss-type claims feature prominently in senior national courts.[6] Identifying the life left in Swiss claims through the patent landscape will shed light on the significance of the courts' Swiss-type claim rulings.

Research Questions

In this paper we examine the European patent landscape of first and further medical uses of known products. Specifically, we address the following research questions:

1) What activity has there been in the EPO for medical uses of known products over the last 30 years?; How many of these patents are granted per year?; and What is their allowance rate?;

2) Which organizations are leading the patent activity for medical uses of known products?; and

3) What types of claim formulations are being used to protect these inventions and what is their relative prevalence?

Search Strategy & Landscaping

We developed a search strategy designed to answer the above questions. The strategy follows the recommendations of Bubela *et al.* on patent landscaping for life sciences innovation[7], as well as the checklist of information for patent landscapes recommended by Smith *et al.*[8] to ensure quality and transparency. Similar methodologies have been used to analyze the patent landscape of gene patents[9,10,11] and other medical-related inventions.[10,12]

A. EPC2000 Claims

Table 1 provides a summary of the search strategy and results. This strategy is designed to identify patents with claims drafted following the canonical claim formulations for patentable subject matter under the current EPO examination guidance for "first or further medical use of known products" (examples B, C, and D, **Box 1**).[13] Claim formulation B has the form "Product X *for use* as a medicament" (where X is known but its use in medicine is not known). This can be used when a patent discloses the first medical use of a known product. It is based on Art. 54(4) EPC. EPO claim formulations C and D are of the form "Product X *for use* in the *treatment of* […]" to claim a further medical use for a known product. These are based on Art. 54(5) EPC.

The search strategy ranges from high sensitivity (**Table 1** Search ID: **S1**) to high specificity to minimize false positives (**Table 1** Search ID: **S8**). Since the three admissible claim formulations all include "for use" the **S1** search strategy is optimized for high sensitivity (but low specificity) and provides a conservative upper-bound of the total number of use-limited product patent applications across all fields over the last 30 years. Specificity is substantially improved by restricting the search to classes focused on medical patents (Cooperative Patent Class-CPC: A61), resulting in 166,679 patent documents (i.e., patent applications and corresponding granted patents) for first and further medical uses of known products (**S2**).

Since the EPO's canonical claims directed to medical uses of known products employ the claim formulations "Product X *for use* as a *medicament*" or "Product X *for use* in the *treatment* of […]", searches **S3-S7** identify these medical use claims with increasing degrees of specificity by requiring the claims to contain "for use" and "medicament" (**S3**, **S5**) or "treat*" (**S4**, **S6**, **S7)** with increasing degrees of proximity and further narrowing the subclass to CPC A61K, which specifically includes medical uses of drugs. This results in an upper bound of 84,696 and a lower bound of 30,439 patent documents. The last search strategy (Search ID: **S8)** is designed to identify with high specificity EPO granted patents containing EPC2000 claims directed to medical uses of known products. The search results indicate that there are at least 13,265 patents granted by the EPO containing claims directed to medical uses of known products.

B. Swiss-Type Claims

A separate search strategy was developed to analyze the use of

Table 1 - Summary of Search Strategy

Search ID	Search Strategy	Number of Patents
S1	ACLM:("for use") AND ISD:([NOW-30years TO 2020-12-31]) in EPO	390,813
S2	ACLM:("for use") AND ISD:([NOW-30years TO 2018-12-31]) AND CPC:A61 (Medical or Veterinary Science) in EPO	166,679
S3	ACLM:("for use" AND medicament) AND ISD:([NOW-30years TO 2020-12-31]) AND CPC:A61 (Medical or Veterinary Science)	84,232
S4	ACLM:("for use" NEAR10 treat*) AND ISD:([NOW-30years TO 2020-12-31]) AND CPC:A61 (Medical or Veterinary Science) in EPO	88,696
S5	ACLM:("for use" NEAR3 medicament*) AND ISD:([NOW-30years TO 2020-12-31]) AND CPC:A61 (Medical or Veterinary Science)	26,748
S6	ACLM:("for use" NEAR3 treat*) AND ISD:([NOW-30years TO 2020-12-31]) AND CPC:A61 (Preparations for medical, dental, or toilet purposes) in EPO	61,049
S7	ACLM:("for use" NEAR3 treat*) AND ISD:([NOW-30years TO 2020-12-31]) AND CPC:A61K CPC:A61K (Preparations for medical …purposes) AND in EPO	30,439
S8	ACLM:("for use" NEAR3 treatment) AND ISD:([NOW-30years TO 2020-12-31]) AND CPC:A61K (Preparations for medical … purposes) AND DT:G in EPO	13,265

Box 1 - EPO Guidance Excerpt

EPO Guidance on claim formulations for First or further medical use of known products

Where the subject-matter of a claim is rendered novel only by a new therapeutic use of a medicament, the claim may no longer have the format of a so-called "Swiss-type" claim as instituted by decision G 5/83 ("Use of a substance or composition X for the manufacture of a medicament for therapeutic application Z") if the application has a filing or earliest priority date of 29 January 2011 or later (see the Notice from the EPO dated 20 September 2010, OJ EPO 2010, 514).

The effect of the different claim formulations on patentability is summarised in the table below:

Examples

#	Claim	Patentable?	Article
A	Use of product X for the treatment of asthma	No	53(c)
B	1. Product X for use as a medicament [X known as e.g. herbicide] 2. Product according to claim 1 for use in the treatment of asthma	Yes (even if X is a known product, but its use in medicine is not known) Yes	54(4)
C	Product X for use in the treatment of cancer*	Yes (even if case B is prior art, provided that such a claim is inventive over B and any other prior art)	54(5)
D	Product X for use in the treatment of leukaemia*	Yes (even if cases B and C are prior art, provided that D is inventive over B and C and any other prior art because leukaemia is a specific type of cancer)	54(5)

* Note: The corresponding Swiss-type claims for cases C and D (required under EPC 1973) would be "The use of Product X for the manufacture of a medicament for the treatment of cancer/leukaemia".

Swiss-type claims. Swiss-type claims have the form "*Use of* a substance or composition X *for the manufacture of a medicament* for therapeutic application Z" or "The *use of* Product X for the manufacture of a medicament for the treatment of […]". Accordingly, they can be identified by searching for "use of" in proximity to "manufacture" (or synonyms) with various degrees of sensitivity and specificity (e.g., "manufacture of a medicament").

Expert Review & Claim Analysis

The most recently granted 500 patents containing medical use claims for known products from **S8** were reviewed by two experts (JL & MJ) in order to further analyze and classify the patents. The purpose of the expert review was to determine the specificity of the search algorithm and to manually classify 500 patents based on their claims (see **Supplementary Information**).

Each patent was reviewed to determine if the EPC2000 "medical use claim" was an independent or dependent claim. As mentioned in the introduction, this is important since *independent claims* directed to medical uses of known products are indicative of drug repurposing activity, but this is not the case if the "medical use" EPC2000 language is found in dependent claims. Based on the expert review the patents containing medical use claims were classified as: 1) "product patents" where the broadest independent claim was directed to a novel compound or substance (although there were dependent claims containing EPC2000 medical use language), 2) "medicament patents" where the broadest independent claim was directed to a "medicament" (first use claim EPO Type B example), 3) "medical use patents" where the broadest independent claim is of the form "Compound X for use in the treatment of disease Y" (i.e., EPC2000 claims), and 4) "excluded" where the broadest independent claim was a method and the EPC2000 claim was dependent.

The expert review indicates that the **S8** search algorithm has an estimated specificity greater than 99.8%, as no false positives were found in the sample of 500 patents. In all instances, there were EPC2000 claims (dependent or independent).

Landscape Results & Discussion

The output of the search strategy was analyzed further using patent analytics to answer the research questions.

1)What activity has there been in the EPO for medical uses of known products over the last 30 years?; How many of these patents are granted per year?; and c) What is their allowance rate?

Our search strategy (**S7**) yielded 30,439 patent applications with claims directed to medical uses of known products (EPC2000 claims). Of these, 13,265 were ultimately granted and published as issued patents over the last 30 years (**S8**).

Fig. 1 shows the patent applications (**S7**) and granted patents (**S8**) from 2001 to 2020. This figure indicates that there has been a substantial upward trend in the last 10 years (since 2010) for patents with EPC2000 claims. The outputs of **S7** and **S8** also permit the calculation of the patent allowance rates. The relative proportion of granted applications to the total number of applications for years with no (or minimal number of) pending

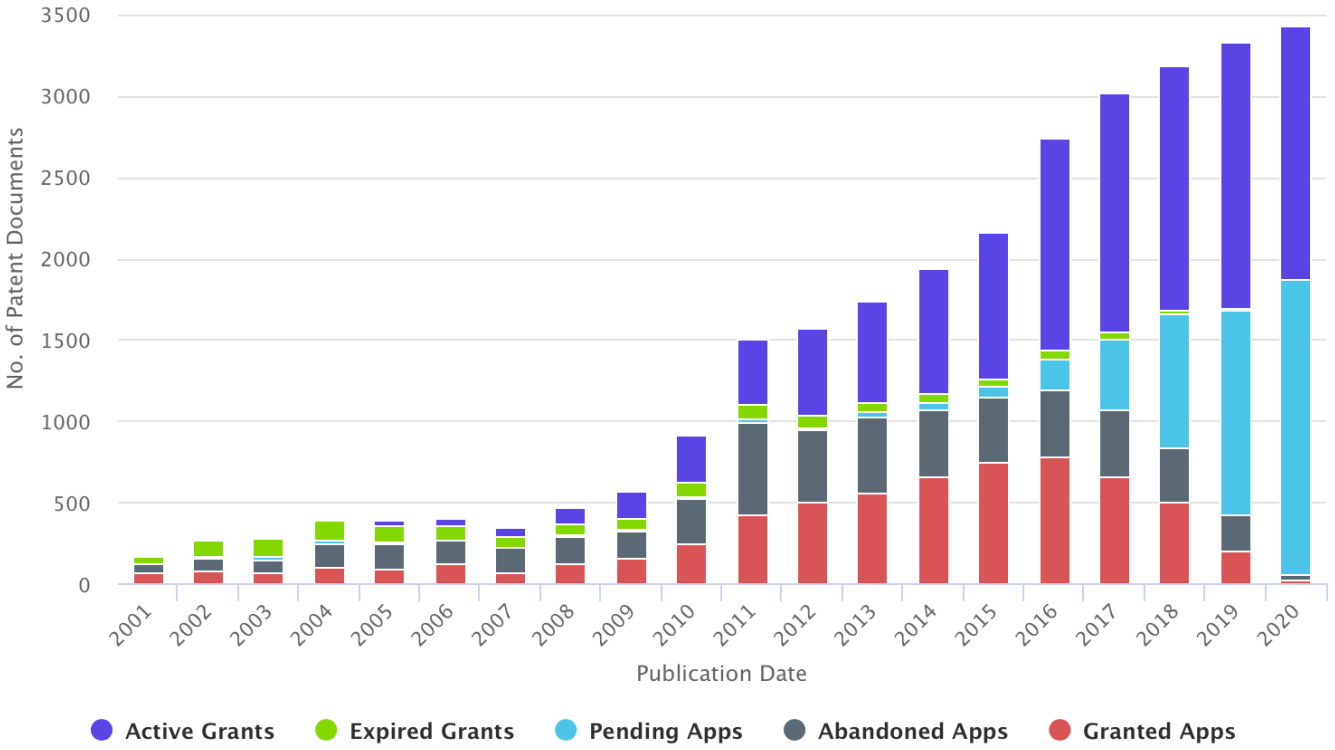

Fig. 1 EPO patent applications and granted patent publications with claims directed to medical uses of known products (EPC2000 claims) from 2001 to 2020 by publication date of the patent application (**S7**). The relative proportion of granted applications (red, **S8**) and abandoned/rejected applications (grey) to the total number of applications for years with minimal number of pending applications (light blue) indicates the patent allowance rate (42% in 2011 to 62% in 2014).

applications indicates the patent allowance rate has steadily increased from 42% in 2011 to 62% in 2014). For comparison, the EPO President Battistelli reported at the 30th Annual US Bar-EPO Liaison Council Meeting in 2014 that EPO patents are granted in 49% of total filings.

For patent applications filed after 2014 there is still a significant proportion of applications with pending status (**Fig. 1**) and consequently allowance rates can only be estimated. That said, for those applications for which there is a final disposition the trend of allowance rates higher than the EPO overall grant rate of 49% continues.

The results of **S8** (granted patents) were further analyzed in order to determine whether the EPC2000 claim was independent or dependent. **Fig. 3** compares the number of granted patents including EPC2000 claims (independent and dependent) with the number of patents with independent EPC2000 claims. The results show that approximately 30% of patents include an independent EPC2000 claim, and that this proportion has been relatively consistent for the last 20 years. This result was confirmed by our expert review of the last 500 patents granted in 2020, which found the EPC2000 medical use claims were the independent claim in 31.6% of the cases. This corresponds to patent protection for drug repurposing activity. Conversely, in approximately 70% of the cases, patent applications for novel products (e.g., compounds and substances) also claimed the medical use in the same application. EPC2000 canonical claim language was employed in these dependent claims.

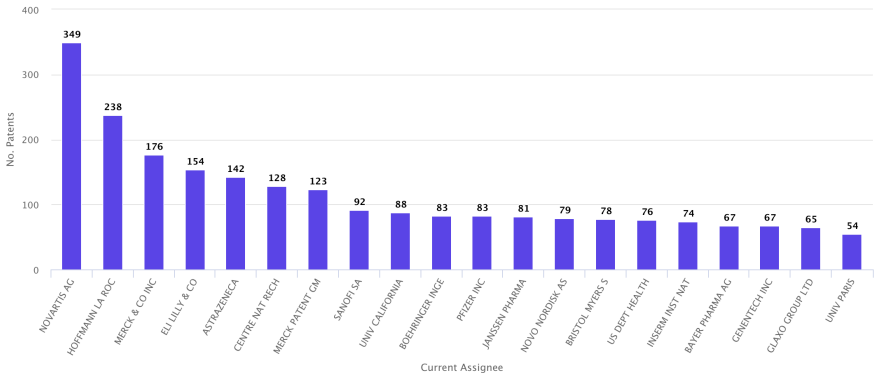

Fig. 2 Organizations with the highest count of patents (**S8**) with EPC2000 claims since 1990. The graph shows the current patent owners (current assignee) and their corresponding number of patents with EPC canonical claim language (independent or dependent claims).

The special novelty rule in Art. 54(4) and Art. 54(5) EPC provides an incentive to disclose medical uses for novel products, since if not claimed along with their novel product (or otherwise made available to the public), third parties could use the special rule to obtain patent protection (and associated exclusivity) for first or further medical uses. To avoid this, patent applicants draft independent claims to protect the product for all uses (e.g., medical or non-medical) and EPC2000 canonical claim language in dependent claims to specifically prevent third parties from obtaining the medical use claims through the special novelty rule. Furthermore if a competitor subsequently proves the compound claim to be invalid, the dependent EPC2000 claim may still be valid. The expert analysis reveals that when the EPC2000 claims were dependent, in approximately 66.2% of cases, the EPC2000 claims were dependent on novel products (e.g., new compounds, compositions, and substances). Since 2017, the EPO has been granting more than 1,500 patents per year with EPC2000 claims (**Fig. 2)**.

2) Which organizations are leading the patent activity for medical uses of known products?

The results of **S8** were analyzed to determine which organizations are leading the patent activity for further medical uses. **Fig 2** provides a summary of these results, showing the 20 top current assignees (patent owners) with the corresponding number of patents granted for medical uses identified by **S8**. The top 20 assignees are dominated by large pharmaceutical companies (e.g., Novartis, Roche, Merck). However, a deeper level of analysis at the claim level (**Fig. 4**) reveals that universities and publicly funded research institutes are leading the activity for patents with independent EPC2000 claims. These organizations are making use of the

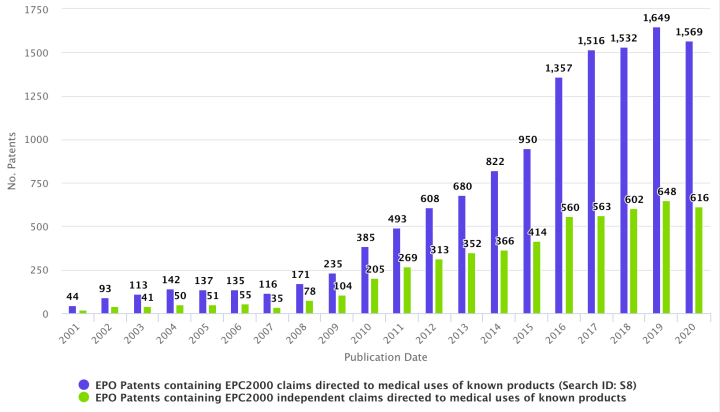

Fig. 3 Granted patents with EPC2000 claims per year. The blue bar shows the count of granted patents with EPC2000 claims (independent or dependent) and the green bar shows the count of patents with independent EPC2000 claims. The results indicate that historically the claims directed to medical uses of known products (EPC2000 claims) are the independent (broadest scope) claims in approximately 30% of the patents (**S8**).

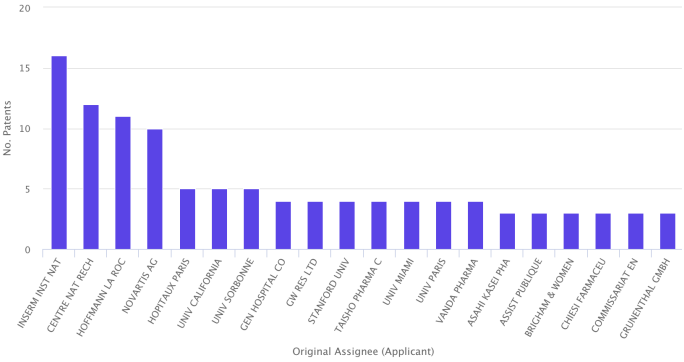

Fig. 4 Organizations leading the inventive patent activity (original applicants/ assignees) resulting in granted patents with independent EPC2000 claims. Comparison with Fig. 2 indicates an increased proportion of university and research institute patent activity.

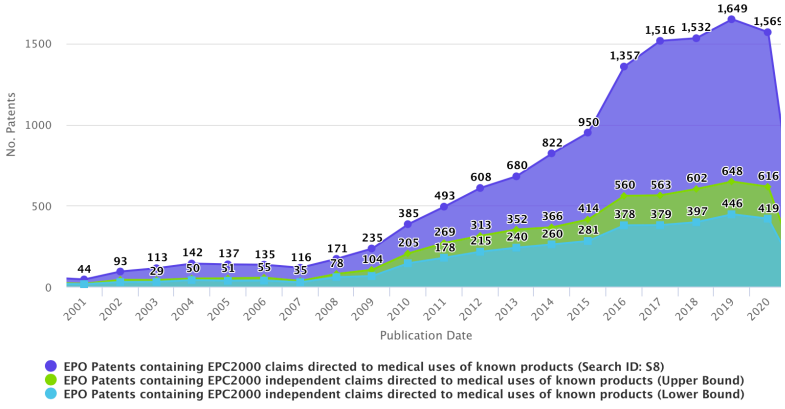

Fig. 5 Granted patents with EPC2000 claims and estimate (upper and lower bounds) for the number of patents whose *broadest* claim is an EPC2000 claim. The upper bound includes patents with EPC2000 claims in any of the independent claims, whereas the lower bound includes patents where the EPC2000 claim is the only independent claim (i.e., the broadest claim in the patent).

EPC2000 canonical claim language to benefit from the Art. 54(4) EPC novelty rule. This indicates that universities and publicly funded research institutes are playing an important inventive role in drug repurposing.

3) What types of claim formulations are being used to protect these inventions (medical uses of known products) and what is their relative prevalence?

Fig. 3 shows the number of granted patents with EPC2000 claims per year (**S8**) and the proportion of these patents that contain independent EPC2000 claims. Our search results indicate that EPC2000 claims are the broadest (independent) claims in 26% to 39% of the cases (**Fig. 5**).

We further analyzed the claim formulations used to protect medical use inventions and their relative prevalence by searching their respective canonical claim language. **Fig. 6** compares EPC2000 claims (in blue) and Swiss-type claims (in green). It shows the dominant claim language for protecting medical uses of known products is now "Product X *for use in the treatment of* disease Y," corresponding to the EPO Guidance examples B.2, C and D, whereas Swiss-type claims were more prevalent until 2011.

EPC2000 vs Swiss-type Claims

Fig. 6 compares the relative prevalence of EPC2000 claims versus Swiss-type claims in granted patents. EPC2000 claims have been more prevalent in the last 10 years. The highest number of granted patents containing Swiss-type claims occurred in 2006. As expected there has been a steady decline of granted patents employing this type of claim drafting after 2011. In 2011, 342 Swiss-type claims were granted, and in 2020 just 30. As explained in the introduction, the Swiss-type claim format is not acceptable for patent applications with a priority date on or after 29 January 2011.

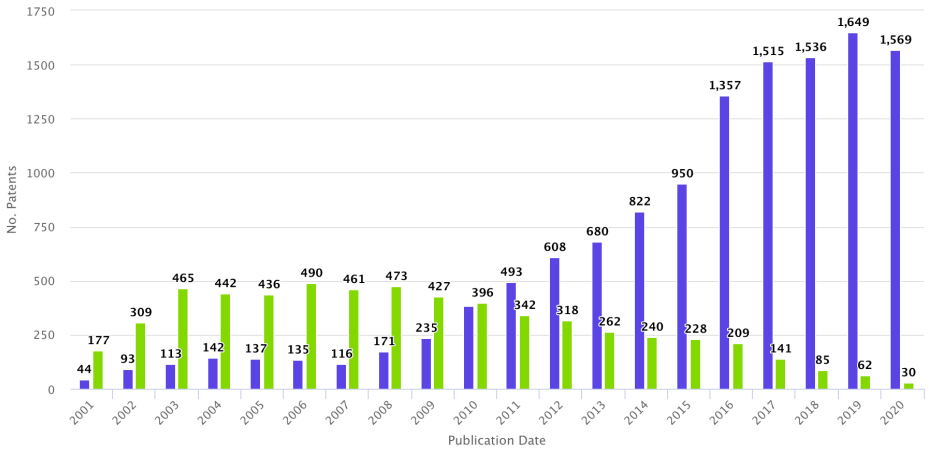

Fig. 6 Types of claim formulations that are being used to protect inventions that claim medical uses of known products (compositions/compounds) and their relative prevalence. Swiss-type claims (green) vs EPC2000 treatment claims (**S8**).

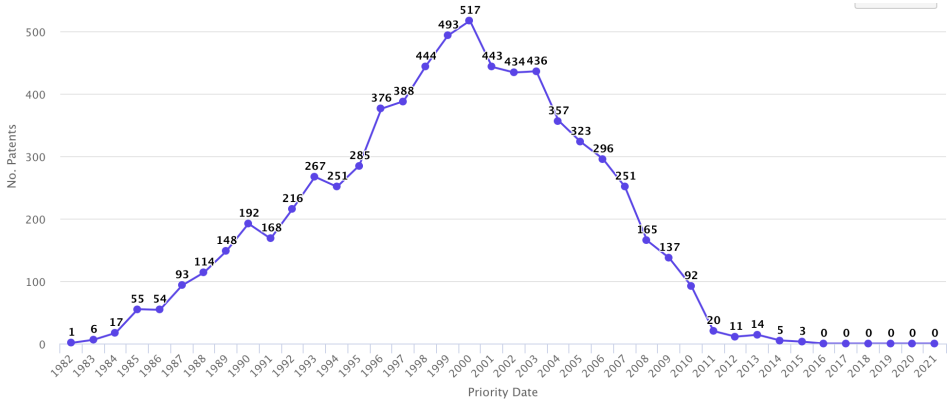

Fig. 7 Priority dates of EPO patents containing "Swiss-type" claims. This type of claim drafting is no longer acceptable for patent applications with priorities dates on or after 29 January 2011.

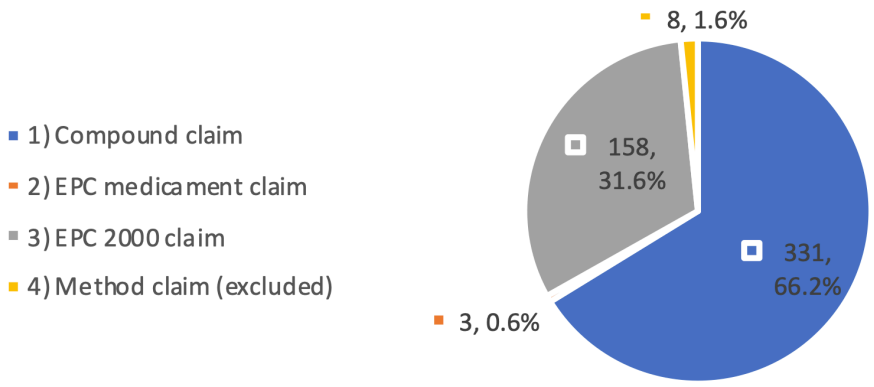

Fig. 8 Classification of patents according to the broadest independent claim: 1) "product patents" (novel compound or substance claims), 2) "medicament patents" (EPC medicament claims), and 3) "medical use" patents (EPC2000 claims). Methods patents (where the independent claim was directed to a method) were excluded.

Swiss-type Claims & Patent Validity

We identified a total of 7,072 granted patents containing Swiss-type claims over the last 30 years. We conducted a further analysis to determine the priority dates of the granted patents containing Swiss-type claims.

Fig. 7 shows a plot of the granted patents containing Swiss-type claims with the time axis changed from publication date (i.e., date of publication of the granted patent) to priority date (i.e., date of the earliest priority claimed by the granted patent). Given the change in the law, patent applications with a priority date on or after 29 January 2011 should not have included Swiss-type claims. Even if inadvertently included in the patent application, the EPO Examiner should have rejected those claims. However **Fig. 7** reveals the existence of applications with priority dates after 2011 and Swiss-type claims.

Our results indicate that out of the 7,072 patents containing Swiss-type claims, 50 have priority dates after 29 January 2011. These claims are thus potentially invalid (if national courts follow the reasoning of the Enlarged Board of Appeal in G02/08). The overall impact on the granted patent depends on whether the improperly granted claims are independent or dependent. Expert review of each of these applications reveals that in 5 of these 50 patents the Swiss-type claims are independent claims. Furthermore, in 2 out of the 5 they are the only independent claims in the patent. Finally, in 1 of these 2 the Swiss-type claim is the sole patent claim. This indicates that at least 2 patents are at risk of being entirely invalidated and 50 have claims that could be invalidated in revocation proceedings.

The slow decline of Swiss-type claims

Fig. 7 shows that more patents with Swiss-type claims have priority dates in 2000 than any other year. Patents have a maximum term of 20 years from their priority date. Thus, all 517 patents granted with a priority date of 2000 have now expired. Yet, 443 patents with Swiss-type claims were granted with priority dates in 2001, and over 400 with priority dates in 2002 and 2003. Many of these patents will still be in force if they have not been invalidated and their annual renewal fees have been paid. Thus recent court decisions on Swiss-type claims (e.g., the 2018 UK Supreme Court decision *Warner-Lambert Co LLC v Generics (UK) Ltd*[6] are relevant for hundreds of patents, and could have commercial significance.

In EPO case law,[14] Swiss-type claims and canonical EPC2000 medical use claims protect different subject matter. Some national courts share this view. For example in the UK, a Swiss-type claim is a method of manufacturing a product for a specific use; whereas an EPC2000 claim is a purpose-limited product. Thus two patents can be obtained by the same applicant with the same priority date without amounting to double patenting. Accordingly, it is generally advisable to pursue both claim types in the same application (as long as the priority date falls before 29 January 2011).

Classification of patents according to the broadest independent claim

Fig. 8 shows the results of the expert classification. An EPC2000 claim is the broadest independent claim in 31.6% of the 500 patents analyzed. In 66.2% of the patents the broadest independent claim is directed to a compound and the medical use claim is dependent. These results confirm the results generated with the automatic search algorithm (**Fig. 3** and **Fig. 5**).

We also found (**Fig. 8**) that medicament claims (EPC2000 Example B) are relatively rare (0.6%). These contain an independent claim to "Compound X *for use* as a *medicament*" (first medical use claims under Art. 54(4) EPC).

Fig. 8 also shows that EPC2000 claims for use in the treatment of specific diseases are the second most sought-after claim for protecting therapeutics. The most sought-after are the initial product claims which protect a novel substance, compound or composition.

New EPC2000 medical uses can be claimed for previously known substances and compositions but not for previously known devices. This follows from the precise words used in the drafting of Art. 54(5) EPC, which provides the legal basis for the novelty of second (or further) medical use claims. The expert analysis did not find examples contrary to this.

The precise words of Art. 54(5) further indicate that an EPC2000 medical use claim is permitted for a substance or composition "for any specific use in a method referred to in Art. 53(c)", as long as the "specific use" is not disclosed in the prior art. Accordingly, EPC2000 new medical use claims are not limited to *treatment* of new diseases. It is also possible to claim a new medical use in *diagnosis* or *surgery*. We saw very few EPC2000 new diagnostic use claims in the expert analysis.

Furthermore, EPO guidance and case law indicates that Article 54(5)'s reference to a new "specific use" does not require a new disease. The use of the known compound for use in the treatment of the same disease may still be a novel therapeutic application if the new group of subjects is distinguished by its pathological or physiological status. A new dosage may also qualify.

Patent Claim Examples

The **Supplementary Information** provides examples from the expert review with patents classified by

their independent claims into 1) product patents, 2) medicament (first medical use) patents, and 3) EPC2000 medical use patents. Additionally, it contains detailed information for each patent including independent and dependent claims, current assignees, original assignees, inventors, priority dates, and citations. This information is provided for 500 of the most recently granted patents containing medical use claims for known products.

Policy Considerations

The results of the study help to allay concerns that the European patent system is failing to provide sufficient incentives for repurposing.[4] More specifically, it assuages concerns that new medical use patents are too hard to obtain. But further research is required for a full assessment of the policy concerns.

Granting Practice

We see no signs that the patent system is failing in the data we have analyzed, notwithstanding the complexity of the European Patent Convention for new medical use patents. On the contrary, our data shows new medical use patents are desired and obtained by universities and publicly funded research institutes, as well as large pharmaceutical companies. This is evident from the results in **Figs. 2-4.** The number of granted patents with independent EPC 2000 claims is increasing, and the total over the past two years is higher than it has ever been. **Fig. 7** reinforces this, showing that nearly 2000 granted Swiss-type claims have priority dates between 2001 and 2011 (the last acceptable year) meaning that they could still be on foot.

It is also very telling that the allowance rate for patents with canonical EPO new medical use claims is between 42% and 62% (compared to the EPO overall allowance rate of 49%). So although it may be difficult in particular applications to show inventive step and/or sufficient teaching in the specification,[4] overall the difficulties are no greater than those experienced in the patent system generally.

Disclosure Incentives & Dissemination of Scientific Information

A third point of note is our finding that a substantial majority of new medical use claims (approximately 70%) are applied for and granted as dependent claims in patents claiming novel products. As explained, we speculate that patent applicants voluntarily disclose uses in this way to prevent third parties from obtaining the medical use claims through the special novelty rule in Art. 54(4) and 54(5). The emerging policy point is that the special novelty rule appears to encourage early disclosure. This shows empirically that the special novelty rule has positive effects and supports the public interest in dissemination of scientific knowledge. To a degree this offsets the criticisms levelled at the special novelty rule for over-privileging the pharmaceutical industry,[15] and slowing generic entry.[2]

Further research is required to assess the overall sufficiency and appropriateness of incentives for repurposing research. It is an important area of pharmaceutical innovation, and several issues remain.

Infringement and Revocation Proceedings

Perhaps the most significant issue is that although EPO *granting* practice for new medical use patents appears to be working normally, arguably systems for *enforcement* are not. Further research could investigate system-wide difficulties in infringement and revocation proceedings.

There are several signs of troubling levels of legal uncertainty and complexity. For instance, although the majority of second medical use patents in Europe are granted by the EPO (as opposed to being granted by national patent offices), questions of infringement and revocation must be brought before the national courts, and this will continue until the Unified Patent Court (UPC) begins operation. As such, national laws must be taken into account for questions of revocation and enforcement.

Decisions by the national courts indicate a variety of views and on-going uncertainty. In the UK, what constitutes infringement of a new medical use claim is still largely unclear when a skinny label carves out the patented use. In litigation over Warner-Lambert's Swiss-type claims for the use of pregabalin in the treatment of pain, the UK Supreme Court held in 2018 that these claims were process claims for *manufacturing* a drug for a particular use, so no-one using the *drug* could be sued for indirect infringement, and doctors and pharmacists could not be liable for direct infringment. However the judges split 2:2:1 on the evidence required to establish direct infringement of a Swiss-type claim by a generic manufacturer, and their opinions on infringement were in any event strictly speaking *obiter* (the patent having been revoked for invalidity). For Lord Sumption and Lord Reed, the outward presentation of the product as it emerges from the manufacturing process is solely relevant; so a skinny label is sufficient to avoid infringing a Swiss-type claim. But two of the remaining judges held that evidence of the defendant's intention is also relevant (and the remaining judge agreed for rare cases), so a skinny label might not be enough. The decision also left many unanswered questions in relation to (direct and indirect) infringement of EPC2000 claims.

An article in 2018 further illustrates the range of views in European national courts, several of which contradict the UK's current

position.[16] The authors argue that the German courts regard Swiss-type claims as essentially use-limited *product* claims despite the language of processing and manufacturing. German courts also take the view that in some circumstances defendants using the drug *can* be liable for *indirect* infringement of a Swiss-type claim. Several countries also examine carefully the defendant's intention. Cuonzo and Ampollini explain that the national courts can reach different decisions because the actions of a defendant may vary in the different health systems.

Patent Protection Incentives & Optimality
A second remaining issue for policy development is that the study we completed did not address whether the patent count is optimal. Arguably large pharmaceutical companies, universities and publicly-funded organizations could be more active in the repurposing arena. A recent study has shown that slightly less than half of all drugs authorised by the European Medicines Agency are repurposed.[17] Another study shows that repurposing activity slows once a generic is authorised.[18] Perhaps repurposing research could be stimulated better in these apparently under-exploited areas if the patent system was modified and more, or fewer, patents were granted.

It might be thought that the relatively high number of patents with independent EPC2000 claims assigned to universities and research institutes (**Fig. 4**) is evidence that the system is not optimized. Arguably, this data indicates that patents are not operating as strong enough incentives to draw pharmaceutical companies into the repurposing space. Otherwise they would constitute the top applicants, as they do in **Fig. 2**. Further research would be necessary to analyse this fully, but there are reasons to doubt the argument. Universities and research institutes could be expected to have relatively high patenting activity for repurposing due to a number of aspects of medical practice, patent law, and drug availability. First, the availability of authorized drugs means that universities have relatively easy access to safe compounds to test against new diseases, and most European countries permit research on the subject matter of a patent, even for commercial purposes. Second, universities and hospitals are often linked, and patents can arise as a consequence of these collaborative medical practices. Physicians can prescribe drugs 'off label' for purposes not authorised by regulatory agencies,[19] and in the right circumstances, they could patent a confirmed off-label purpose or an interesting clinical side effect as a new medical use. Third, governments are actively encouraging academic centres to pursue repurposing.

Conclusion

This study addressed three core research questions set out in the introduction. Our results show that (1) EPC2000 claims are in demand. After primary product claims for novel substances or compositions, they are the most sought-after patent claims to protect therapeutics. The number of EPC2000 patents has steadily increased since 2010. Their allowance rate has also steadily increased from 42% in 2011 to 62% in 2014. For patent applications filed after 2014, a significant proportion of applications are still pending, and consequently allowance rates can only be estimated. That said, for those applications for which there is a final disposition, the trend of allowance rates higher than the EPO overall grant rate of 49% continues. We found at least 13,265 patents claiming medical uses of known products. Furthermore, in approximately 30% of the cases the medical use claims are the independent (broadest scope) claims of the granted patent. Expert review of the claims from the most recently granted 500 patents confirmed this. These independent EPC2000 claims are indicative of patent protection for drug repurposing.

Our results also show that (2) the organizations with the largest patent portfolios containing claims (independent or dependent) directed to medical uses of known products since 1990 are primarily large pharmaceutical companies. However, when the results are analyzed based on the original assignees for patents with *independent* medical use claims, we find that universities and research institutes have led this inventive activity.

We also identified (3) a total of 7,072 granted patents containing Swiss-type claims over the last 30 years. As expected, Swiss-type claims have been declining since 2011. Although no longer acceptable since 29 January 2011, we identified 50 granted patents with Swiss-type claims and priority dates after this date. Accordingly, these patents have claims at risk of invalidation. We found over 2000 patents with Swiss-type claims with priority dates after 2001 and before 2011. Assuming payment of the maintenance fees, these patents are still in force and case law affecting Swiss-type claims, such as *Warner-Lambert*, is still relevant and is likely to remain commercially significant for several more years.

These results have significant policy relevance for the field of pharmaceutical innovation known as drug repurposing. The development of novel therapeutic applications for known drugs (repurposing) is generally considered a desirable goal. The patent system can support or hinder repurposing activity. Our study reveals that new uses of known drugs can be protected with sufficient legal certainty at the EPO. Law and guidance is clear for those prosecuting such patents. Coupled with the increasing rates of granted

EPC2000 patents, their corresponding allowance rates, a comparison with patent allowance rates in other technical fields, significant numbers of residual Swiss-type claims and the diversity (private and public sector organizations) of patent owners, these findings strongly suggest that there is no major policy challenge in obtaining patent protection for new medical uses of known products. This first-of-kind evidence-based study demonstrates this finding empirically using patent landscaping and analytics. Provided that the new treatment indication is novel, first, second and subsequent medical uses of known compositions or substances are patentable as purpose-limited products. They are also patentable for several more years as Swiss-type claims (assuming a priority date before 29 January 2011).

If repurposing research is lagging, it seems other factors are in play; factors other than the dynamics of prosecuting new medical use patents. It is possible that the law on patent infringement is part of the issue. Litigation to enforce patents currently takes place before national courts, which have significantly different views on the (direct and indirect) infringement of second medical use claims. The legal uncertainty this creates may be hindering repurposing research. A (largely) unified position is likely to emerge once the Unified Patent Court is established. But legal principles at a pan-European level may have their own challenges. European countries have different national healthcare systems and their own cultures for drug procurement and tendering, medical prescribing including 'off-label use', dispensing and drug substitution by pharmacists, and systems for flagging patent protection. These issues would benefit from further research.

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Competing interests

The authors declare no competing interests.

Additional Information

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