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Joint USPTO-FDA Collaboration Initiatives Listening Session.

I would like to commend, again, the U.S Food and Drug Administration (FDA) and the U.S Patent and Trademark Office for the listening session and the opportunity for public interest groups and patients to provide comment on proposed initiatives.

Further to earlier comments submitted and orally presented at the listening session in person on 19 January, 2023, I would like to provide the following additional observations.

1. Average Period of Market Exclusivity for FDA Approved Drugs

Comments submitted by the Biotechnology Innovation Organization (BIO) and Mr. Salsberg of Novartis pointed to the average period of market exclusivity for FDA approved new-molecular entity based drugs from 1995-2019 was between 12.2 years and 14.6 years. What was noticeably absent from the sources cited by Mr. Salsberg and BIO (which incidentally represents the biologics industry) was the average period of market exclusivity for biologic drugs on the U.S market.

Based on our calculation of 8 of the leading biologics on the U.S market to date, as shown in the table below, we found that the average period of market exclusivity was 19 years – and a median of 20.2 years – before a biosimilar enters.

Branded Biologic Product	First FDA approval date	Years on the U.S. maket	Biosimilar approved by FDA	Biosimilar on the market	Date of first biosimilar launch	Years of branded exclusivity
Humira	Dec, 2002	20.1	✔	✔	Jan, 2023	20.1
Avastin	Feb, 2004	18.9	✔	✔	Jun, 2019	15.3
Rituxan	Nov, 1997	25.2	✔	✔	Oct, 2019	21.9
Herceptin	Sep, 1998	24.4	✔	✔	Jun, 2019	20.7
Remicade	Aug, 1998	24.5	✔	✔	Oct, 2016	18.2
Lantus	Apr, 2000	22.8	✔	✔	Aug, 2020	20.3
Eylea	Nov, 2011	11.2	✗	✗	-	11.2
Enbrel	Nov, 1998	24.3	✔	✗	-	24.3
ave		**21.4**				**19.0**
median		**23.5**				**20.2**

Given the dozens and often hundreds of patents that protect biologic drugs (and also small molecule drugs), it is clear to see that companies are using the patent thicket strategy to get as close to or above 20 years of actual patent protected market exclusivity once a drug is approved.[1] Without the patent thickets that protected the drugs highlighted in the table above, we could potentially have seen biosimilar entry much earlier, approximately after 14-15 years of market exclusivity.

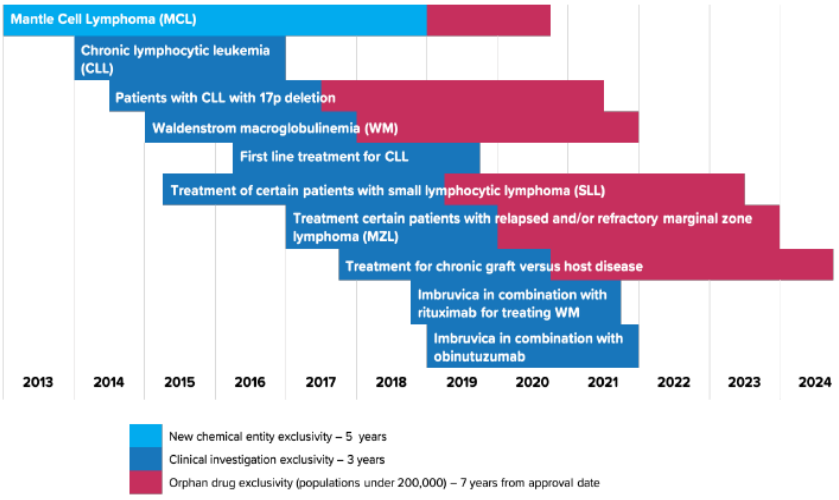
It is important to note here that the patent system provides 20 years of patent protection for an invention – not 20 years of patent protected market exclusivity. This 20 year patent period from the date of filing a patent application covers the development time to bring the product to market and any market exclusivity once the product is approved. However, as seems to be implied in Mr. Salsberg's comments that were submitted to the listening session (see page

[1] See https://drugpatentbook.i-mak.org/

4), Novartis seems to think that the patent system should be providing 20 years of patent protected market exclusivity once a product is approved.

This is so even though pharmaceutical companies already receive guaranteed separate FDA market exclusivities that can be 7.5 years for small molecule drugs (factoring in the 30 months litigation stay under Hatch Waxman) and 12 years for biologics. An example of the separate FDA exclusivities on the small molecule drug Imbruvica is illustrated below for the drug Imbruvica[2].

- Imbruvica's first FDA exclusivity was the 5-year new chemical entity marketing exclusivity for mantle cell lymphoma in 2013. This marketing exclusivity expired in 2018.
- Eight 3-year clinical investigation exclusivities (CIEs) have been granted for Imbruvica in relation to each subsequent approved indication. Five CIEs have expired; three CIEs are currently in force and expire between August 2020 and January 2022.
- Orphan Drug Exclusivities (ODE) for Imbruvica, which are given for products that treat indications affecting fewer than 200,000 people, have been granted for eight indications and expire between January 2020 and August 2024.



In addition to these FDA exclusivities, AbbVie has filed 195 patent applications associated with Imbruvica, of which 96 have been granted to date. Imbruvica has 29 years of patent protection from December 2006 to March 2036. Despite litigating AbbVie's patent on

[2] https://www.i-mak.org/imbruvica/.

Imbruvica, six generic companies have entered into settlement agreements. As a result of these agreements, competitors will delay introduction of generic versions until 2032 and 2033. This is five to six years after AbbVie's main patents expire on Imbruvica in 2026. These additional years will cost Americans billions more dollars on branded Imbruvica. Even if AbbVie was not able to realise the full 29 years of patent protection it has accumulated on Imbruvica, the thicket of patents have delayed generic entry and will have provided it with a total market and patent exclusivity of at least 18-19 years since the drug was approved in November 2013.

Given that each year of market exclusivity can be worth billions of dollars to companies, the current patent system provides every incentive for companies to build patent thickets in the hope they can extract as close to or above 20 years of patent protected market exclusivity wherever possible. In essence, pharmaceutical companies have found ways to manufacture 20 years of patent protected market exclusivity wherever they can get away it and are putting untold strain and hardship on patients and payers. This is a manipulation of the patent system, which is in urgent need of correction.

2. Whose Patent Data is Reliable?

In their comments, Mr. Mossoff and Mr. Salsberg have presented arguments that the patent numbers and data I-MAK has made available on some of the top selling drugs in the U.S to date is unreliable. This is despite I-MAK making its patent data on a number of drugs it has studied available for review and comment at https://drugpatentbook.i-mak.org/. To date we have not received any feedback from Mr. Mossoff or Mr. Salsberg. Instead, they have preferred to peddle criticisms of our data without providing any evidence to the contrary that the patent numbers amassed by the companies we have presented are incorrect. This is highly unfortunate considering Mr. Mossoff and Mr. Salsberg claim to be believers in "evidence-based policymaking".

According to Mr Mossoff's limited analysis, the only patents that matter in the universe of pharmaceuticals are those listed on the Orange Book (he does not even consider biologic drugs in his analysis as that patent data is only available in a very limited way on the Purple Book). As any seasoned practicing attorney in this field would know, the FDA does not require branded drugmakers to list all their patents in relation to a product. For example, patents

covering metabolites, the process or intermediate compound for making a drug are not required to be listed. To quote Marianne S. Terrot, Associate Chief Counsel for the FDA:

"Orange Book users should **not** rely on an Orange Book patent listing to identify the complete range of patent claims that may be asserted by an NDA holder or patent owner. Not all patents potentially relevant to a product are required to be listed (e.g. methods of making a drug product). *Pending patent applications are not listed* [emphasis added].[3]

In his submission and comments Mr. Mossoff highlighted the "vast" discrepancy in the patent numbers provided by I-MAK for the drug Lyrica as compared to the three listed on the Orange Book. Attached in a separate document to this comment is a schedule of all the 118 patent applications we have identified that relate to the drug Lyrica (pregabalin), 64 of which are granted.[4] The patent landscape includes close analogs of the compound pregabalin, the active ingredient in Lyrica, because pharmaceutical companies use such derivative compounds to block off competitors from producing a similar "me-too" product. As such, these patents are equally as relevant to the strategy for protecting the product from competition as the patents that cover the actual product. While all these granted patents may not have realised the full patent protection term they covered, the fact remains that the difference in the number of patents accumulated on the product Lyrica are on the scale of an order of magnitude considerably more than what is listed on the Orange Book that Mr. Mossoff relies upon.

In the real world of the pharmaceutical business, these patents all form part of a hidden legal strategy, irrespective of whether they are enforced or actually result in longer protection. If they were not of relevance, then why were they filed? A similar question can be asked of Novartis and why they filed and abandoned 44 patent applications on their drug Gleevec? Despite Mr Salsberg's comment that this makes Novartis, anti-patent, the truth lies

[3] Marianne S. Terrot, Overview of the Orange Book and the Off-Patent/Off Exclusivity List available at https://www.wipo.int/edocs/mdocs/scp/en/scp_31/scp_31_h_orange.pdf

[4] In our initial report we had stated there were 68 granted patents, but a subsequent review identified 4 granted patents that did not relate to (Lyrica) pregabalin.

elsewhere. Behind every patent application, pending, granted or abandoned is a strategy. Otherwise why re-apply 44 times?

I-MAK welcomes comment on its patent data. As an organization we are committed to transparency and evidence based – not industry based – policymaking.

Sincerely

Tahir Amin

Co-Executive Director