

“Unofficial” CN Orange Book user guide for pharmaceutical patents (November 2022 ver.)

Abstract

The equivalence of the US Orange Book in China, the “CN Orange Book” has been operating since 29 June 2021. This “CN Orange Book” is a mountain full of treasures, for example clear indication on what claim is covering which subject matter in a particular drug patent. This “unofficial” user guide aims to provide foreigners information on how to navigate this “CN Orange Book”, which operates in Chinese. This is the only tool available to a new drug owner to delay approval of the corresponding generic drugs marketing approval process, as China does not provide new drug/biologic exclusivity.

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“Unofficial” CN Orange Book user guide for pharmaceutical patents (November 2022 ver.)

In the US, the Orange Book is a publication from the US FDA that identifies drug products with marketing approval from the FDA and related patent and exclusivity information. Information in the Orange Book could be used in actions under the Hatch-Waxman Act, which allows a patentee to file an artificial act of infringement that allows the drug innovator to file suit before the generic drug is commercialized, such that the drug marketing approval process of the generic drug at the US FDA could be suspended.

China is required to introduce a similar system under the Phase-I Trade Agreements signed with the US in January 2020. I have been following this since then, and have several articles and posts on this topic. Recently, this “CN Orange Book” (official name: China listed drugs patent information registration platform) has become officially online on 29 June 2021, with many developments thereafter, and I have received many questions on how to use this. This motivates me to write this “unofficial” user guide, mainly for foreign users. This user guide may need updates periodically as things are changing too fast in China.

This drug patent linkage system is the only tool available to a new drug owner to delay approval of the corresponding generic drugs marketing approval process, as China does not provide new drug exclusivity (5 years for chemical, and 12 years for biologic) as in the US at present (may change after the Implementation Rules of the China Drug Administration Law comes into force in the future).

The equivalence of the US FDA in China is the China National Medical Products Administration, the NMPA.

This is the June 2022 version of this guide, as there have been many developments regarding the first drug patent linkage decisions after my various versions below:

- first July 2021 version finished on 19 July 2021;
- second October 2021 version finished on 14 October 2021;
- third December 2021 version finished on 5 December 2021;
- fourth June 2022 version finished on 23 June 2022; and

- fifth November 2022 version finished on 20 November 2022.

Available to anyone, but could only search in Chinese

The “CN Orange Book” is available at <https://zldj.cde.org.cn/home>. Anyone can access information therein. Below is a screen shot of the first page showing different functions thereon:



For searching drug patent information already registered, the information is divided into three tabs, each respectively directed to Chinese medicine, chemical drug, and biological drugs as shown below (with the tab of chemical drugs chosen):

中国上市药品专利信息登记平台

Chinese medicine

Chemical drugs

Biological drugs

当前位置: 首页 > 专利信息公示列表 > 化药专利信息公示列表

中药专利信息公示

化药专利信息公示

生物制品专利信息公示

药品名称:

请输入药品名称

批准文号/注册证号:

请输入批准文号/注册证号

规格:

请输入规格

剂型:

请输入剂型

Q 查找

序号	批准文号/注册证号	药品类型	药品名称	规格	剂型	操作
1	国药准字J20190024	化学药品	盐酸芬戈莫德胶囊	0.5mg (按C19H33NO2计)	胶囊剂	查看
2	国药准字J20190002	化学药品	沙库巴曲缬沙坦钠片	以沙库巴曲缬沙坦计100mg(...	片剂	查看
3	国药准字J20190001	化学药品	沙库巴曲缬沙坦钠片	以沙库巴曲缬沙坦计50mg(...	片剂	查看
4	国药准字J20180077	化学药品	利伐沙班片	20 mg	片剂	查看
5	国药准字J20180076	化学药品	利伐沙班片	15 mg	片剂	查看
6	国药准字J20180075	化学药品	利伐沙班片	10 mg	片剂	查看
7	国药准字J20180021	化学药品	利司那肽注射液	10μg剂量注射笔 (绿色) : ...	注射剂	查看
8	国药准字J20180020	化学药品	利司那肽注射液	20μg剂量注射笔 (深紫红色...	注射剂	查看
9	国药准字J20171054	化学药品	沙库巴曲缬沙坦钠片	以沙库巴曲缬沙坦计100mg(...	片剂	查看

共 448 条

10条/页

< 1 2 3 4 5 6 ... 45 >

前往 1 页

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Searches could be done and directed to the drug name, the format of the drug, dosage, and the drug marketing number at the NMPA. Mostly the name of the drug is used. Partial search for drug patent information already registered is available, but could only be done in Chinese. For example, using only the last three words of Palbociclib in Chinese (“柏西利” in “哌柏西利”) resulted in the following search results:

当前位置: 首页 > 专利信息公示列表 > 化药专利信息公示列表

中药专利信息公示 化药专利信息公示 生物制品专利信息公示

药品名称: 柏西利  批准文号/注册证号: 请输入批准文号/注册证号 规格: 请输入规格 剂型: 请输入剂型 [Q 查找](#)

序号	批准文号/注册证号	药品类型	药品名称	规格	剂型	操作
1	H20180042	化学药品	哌柏西利胶囊	100mg	胶囊剂	查看
2	H20180041	化学药品	哌柏西利胶囊	75mg	胶囊剂	查看
3	H20180040	化学药品	哌柏西利胶囊	125mg	胶囊剂	查看

共 3 条 10条/页 < 1 > 前往 1 页

Extensive information contained therein – good for FTO research

The “CN Orange Book” has the following number of entries as of different dates in the table below:

Type of drugs	30 Jun 2021	19 Jul 2021	3 Oct 2021	5 Dec 2021	20 Nov 2022
Chinese medicines	30	143	243	280	334
Chemical drugs	278	448	532	568	669
Biological drugs	39	60	78	80	110

There was a relatively big surge in July 2021, shortly after the database was firstly introduced on 29 June 2021, while the number of registrations slowed down significantly thereafter, particularly after October 2021. This could be expected, as every drug owner would rush into the register at the beginning.

One amazing feature of the “CN Orange Book” is the inclusion of extensive information in each entry. Below is a screenshot of the entry in the “CN Orange Book” for the drug Palbociclib capsule 125mg (Note: only part of the entries of one of the three patents registered for this drug is shown below due to limit of the screen shot that could be taken):

专利信息登记详情

相关专利号: ZL03802556.6  CN patent no. 专利名称: 2-(吡啶-2-基氨基)-吡啶并[2,3-d]嘧啶-7-酮

专利权人: 沃尼尔·朗伯有限责任公司 专利被许可人:

专利授权日期: 2011-06-22

授权证明文件: 文件1: CN03802556.6_专利证书.pdf
文件2: CN03802556.6授权文本.pdf  click to instantly download CN grant publication

上市许可持有人与专利权人关系: 普通实施许可合同的被许可人

序号	权利要求编号	专利类型	专利保护期届满日	状态	备注
1	1-2	化学药品活性成分化合物专利	2023-01-09	有效	权利要求编号是按本专利无效宣告请求审查决定中维持有效的权利要求编号
2	3	化学药品医药用途专利	2023-01-09	有效	权利要求编号是按本专利无效宣告请求审查决定中维持有效的权利要求编号
		化学药品医药用途专利			权利要求编号是按本专利无效宣告

It can be seen that in addition to the patent number, the following information in the “CN Orange Book” database entries is also available:

- 1) The granted patent itself is available for downloading at a link on the same page.
- 2) The claim number(s), and the relevant subject matter, are clearly identified.
- 3) The full-term expiry of the patent(s) is clearly identified.
- 4) Whether the patent has survived through invalidation is also specified in the note section.

On the other hand, there exists entries without the above extensive information of 1)-4), as shown below as of 19 July 2021:

专利信息登记详情

专利信息

相关专利号: ZL03821144.0

专利名称: 包含盐酸伐地那非三水合物的药物

专利权人: 拜耳知识产权有限责任公司

专利被许可人:

专利授权日期: 2010-12-15

授权证明文件: [文件1: 伐地那非片-ZL03821144.0-专利证书.pdf](#)
[文件2: 伐地那非片-ZL03821144.0-法律状态.pdf](#)
[文件3: 伐地那非片-ZL03821144.0-说明书权利要求书摘要.pdf](#)

上市许可持有人与专利权人的关系: 普通实施许可合同的被许可人

药品与相关专利权利要求的对应关系:

序号	权利要求项编号	专利类型	专利保护期限满日	状态	备注
1					

上市许可持有人联系信息

境内联系人: 刘红强

境内联系电话: 010-65893290

× 关闭

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The same entry above has its information updated as of 3 October 2021, indicating claims 5 to 8 of the relevant patent CN ZL03821144.0 are directed to the drug composition containing the active pharmaceutical ingredient API vardenafil hydrochloride trihydrate:

专利信息登记详情

相关专利号: ZL03821144.0

专利名称: 包含盐酸伐地那非三水合物的药物

专利权人: 拜耳知识产权有限责任公司

专利被许可人:

专利授权日期: 2010-12-15

授权证明文件: 文件1: 伐地那非片-ZL03821144.0-说明书权利要求书摘要 .pdf

文件2: 伐地那非片-ZL03821144.0-专利证书.pdf

文件3: 伐地那非片-ZL03821144.0-法律状态.pdf

上市许可持有人与专利权人的关系: 普通实施许可合同的被许可人

药品与相关专利权利要求的对应关系:

序号	权利要求项编号	专利类型	专利保护期限满日	状态	备注
1	5-8	化学药品含活性成分的药物组合专利	2023-07-03	有效	

上市许可持有人联系信息

境内联系人: 刘红强

境内联系电话: 010-65893290

Updated patent claim information

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关闭

It should be noted that the relevant regulations, the NMPA Measures (see below), put the onus on the patentee/drug marketing approval holder DMAH to ensure the accuracy of the information registered on the platform, which requires the claim(s) covering what aspect of the drug to be identified (Article 4 of the NMPA Measures). Failure to do so could be legally liable (Article 15 of the NMPA Measures), while it is unclear what exactly are the punishments.

Most of the entries in the “CN Orange Book” contain extensive information like the one of Palbociclib capsule 125mg above (if not, updated could be expected). Such information could be very useful for a freedom-to-operate (FTO) exercise. The immediate availabilities of the grant patent publication and the full-term expiry are already very useful. The specific identifications of the claim(s) and relevant subject matter are even more so.

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By contrast, the equivalent FDA records only contain the US patent numbers and the full-term expiry date, but nothing further. Below is the screenshot of Palbociclib capsule 125mg in the US FDA Orange Book records:

Patent and Exclusivity for: N207103

Product 003
PALBOCICLIB (IBRANCE) CAPSULE 125MG

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
003	6936612	01/16/2023	DS	DP			02/26/2015
003	7208489	01/16/2023	DS	DP		Y	02/26/2015
003	7456168	01/16/2023			U-1998 U-2515		02/26/2015
003	10723730	02/08/2034	DS	DP			08/27/2020
003	RE47739	03/05/2027	DS	DP			12/19/2019

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

Restrictions on the type of patents that could be registered

The “CN Orange Book” restricts that only the following types of patents could be registered for the respective drugs (Articles 5 and 12 of the NMPA Measures):

- Chemical drugs – chemical compound of the active ingredient; composition comprising the active ingredient; medical use
- Biological drug – sequence structure of the active ingredient; medical use
- Chinese medicine – composition; extracts from Chinese medicine; medical use

As biologics are also included in the Chinese platform, such is in fact a combination of the US Orange (for chemicals) and Purple (for biologics) Books.

While not specified in the articles of the NMPA measures, the accompanying explanations of the NMPA measures specify that patents covering intermediates, metabolites, crystal form, method of manufacturing and testing methods are **not** considered as relevant patents under the patent linkage system, i.e. these patents should not be registered on the “CN Orange Book”. Therefore, the above types of patents would not be seen in the “CN Orange Book”.

Having said so, one way to get around the restriction on crystal form is to record a patent having a composition claim, or medical use claims (in the form of Swiss-type claim, as method of treatment is not patentable in China) containing the crystal form of the API. An example will be shown below in the first contentious drug patent linkage declaration.

Only Chinese company could register, and make entries on the platform

While everyone could access the platform to view information therein, in order to register entries on the platform (either for a drug, or making a declaration against a drug), one must register as a user on the platform. However, only a Chinese company could do so, as it is required to input the so-called "unified social credit codes" (compulsory) during registration, which are available to all Chinese companies. Further, the registration requires a CN mobile number to complete (for receiving a confirmatory text message). See the screenshot below:

The screenshot shows the '法人注册' (Legal Entity Registration) page on the '国家药品监督管理局网上办事大厅 V2.0' (NMPA Online Service Hall V2.0). The page is titled '全国一体化在线政务服务平台' (National Integrated Online Government Service Platform). The registration process is divided into three steps: 1. 填写认证信息 (Fill in authentication information), 2. 创建用户 (Create user), and 3. 完成注册 (Complete registration). The first step is active, showing a form with the following fields:

- * 法人名称: 请输入您的法人名称 (企业/事业单位/社会组织名称)
- * 法人类型: 请选择法人类型
- * 统一社会信用代码: 请输入法人统一社会信用代码 Unified social credit code
- * 法定代表人: 请输入法定代表人姓名
- * 法定代表人证件类型: 请选择法定代表人证件类型
- * 法定代表人证件号码: 请输入法定代表人证件号码
- * 法定代表人手机号: 请输入法定代表人手机号(中国大陆手机号) CN mobile number
- * 图形验证码: 请输入右侧图形验证码, 再获取短信验证码
- * 短信验证码: 请输入收到的短信验证码

At the bottom, there is a checkbox labeled '我已阅读并同意《政务服务大厅注册协议》' (I have read and agree to the 'Government Service Hall Registration Agreement') and a '开始认证' (Start authentication) button.

Types of declaration from a generic drug applicant against an innovative drug

For details on how such a declaration works, please refer to my articles below:

<https://www.linkedin.com/pulse/cn-patent-inkage-measures-trial-finalized-issued-nmpa-toby-mak> (This article talks about the finalized NMPA measures, which is based on the draft measures below)

<https://www.linkedin.com/pulse/cn-drug-patent-registration-system-orange-book-opened-toby-mak> (This article talks about the draft NMPA measures)

As a summary, when a generic drug applicant applies for drug marketing approval at the NMPA, the generic drug applicant is required to make a declaration of any one of the following four types:

1. That there is no patent information registered related to the drug.
2. That the patent(s) has already expired, or been declared invalid.
3. The date on which the patent(s) will expire, and that generic applicant promises that the generic drug will not go on the market until the expiry of the patent(s).
4. That the patent(s) is not infringed, or should be declared invalid.

As of 20 November 2022, 3182 declarations have been filed, 14 June 2022, 1095 declarations have been announced on the CN platform, showing a significant increase from the following:

- 14 June 2022 – 1095 declarations;
- 5 December 2021 – 745 declarations; and
- 3 October 2021 – 410 declarations.

The vast majority of the declarations are types 1 to 3 declarations. The first type 3 declaration was announced on 9 July 2021, with the screen shot below:

专利声明详情

申请人: 北京泰德制药有限公司
 联系人: 张雨山
 电子邮箱: zhangyush3@tidepharm.com
 通讯地址: 北京市北京经济技术开发区科创八街19号院
 联系电话: 010-67880648-1524

被仿制药等相关信息

药品名称: 哌柏西利胶囊 Name of drug
 持有人名称: Pfizer Europe MA EEIG Owner's name
 批准文号/注册证号: H20180040 Innovative drug registration no.

Type of declaration filed

序号	登记的专利号	登记的权利要求编号	专利声明类型	备注
1	ZL201010255766.6	1-4,5-6,9	3类	
2	ZL201110115074.6	1-2	3类	
3	ZL03802556.6	1-2,3,4	3类	

专利声明类型: 1类: 中国上市药品专利信息登记平台中没有被仿制药相关专利信息(专利信息登记平台登记号、登记的专利号均填写“无”); 2类: 中国上市药品专利信息登记平台收录的被仿制药相关专利权已终止或者被宣告无效, 或者仿制药申请人已获得专利权人相关专利实施许可(在备注中注明相应的具体情形); 3类: 中国上市药品专利信息登记平台收录有被仿制药相关专利, 仿制药申请人承诺在相应专利权有效期届满之前所申请的仿制药暂不上市; 4.1类: 中国上市药品专利信息登记平台收录的被仿制药相关专利权应当被宣告无效; 4.2类: 仿制药未落入中国上市药品专利信息登记平台收录的被仿制药相关专利权保护范围。

Declaration type 4.1 - the patent(s) should be declared invalid
 Declaration type 4.2 - the generic drug does NOT fall within the scope of the patent(s)

× 关闭

The key is the type of the declaration filed, in the screen shot above being type 3. It should also be noted that this page subdivides declaration type 4 into the following two subtypes:

- 4.1 - The patent(s) should be declared invalid.
- 4.2 – The generic drug does not fall within the scope of the patent(s).

The type of the declaration determines whether the drug patentee/DMAH could take action against the subject generic drug marketing approval application. It appears only action could be taken against declaration type 4.2 (the generic drug does not fall within the scope of the patent(s)). While Article 7 of the NMPA measures could be literally read as allowing complaints to be filed at a court or the China National Intellectual Property Administration (the CNIPA) for all 4 types of declarations, when combining with the relevant measures of the Supreme People's Court and the CNIPA, it appears that there is a typographical error in Article 7 of the NMPA measures, and complaint could only be filed for declaration type 4.2.

Therefore, if a generic drug applicant filed a type 4.1 declaration, and even if the generic drug applicant did not file a subsequent invalidation petition, the drug marketing approval process would still proceed as normal by the NMPA as if drug patent linkage protection does not exist.

On the other hand, if the generic drug applicant did file a subsequent invalidation petition and could successfully invalidate the patent, a 12-months exclusivity period would be offered to the first successful challenger, i.e., drug marketing approval would not be granted to another generic drug applicant during this 12-months period.

专利声明详情

×

化学仿制药/中药同名同方药/生物类似药信息

药品名称: 替格瑞洛片

剂型: 片剂

申请人: 山西德元堂药业有限公司

联系人: 段陈平

电子邮箱: dcp207@126.com

药品类型: 化学药品

规格: 90mg

通讯地址: 山西省晋中市山西示范区晋中开发区汇通产业园区开发
区机械园

联系电话: 0354-3072288-805

被仿制药等相关信息

药品名称: 替格瑞洛片

批准文号/注册证号: 大包装注册证号: H20171080/小包装注册证号: H201
71079

持有人名称: AstraZeneca AB

序号	登记的专利号	登记的权利要求项编号	专利声明类型	备注
1	无	无	4.1类	无

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关闭

The first type 4.2 declaration

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hyperlipidemia, dyslipidemia, obesity, hypertriglyceridemia, or diabetic complications (claim 9).

- 3) CN201210201489.X (full term expiry 21 March 2028) - specific formulation comprising the API in the form of dapagliflozin propylene glycol hydrate with a specific dosage regime (claim 1), with further components including bulking agent, binder, disintegrant, and so on (claims 2 and 3), and the medical uses of such specific formulation (Swiss-type claims) for treating diabetes.

For 2), it should be noted that the patent is in fact directed to the crystal form of the API in the form of dapagliflozin propylene glycol hydrate, and therefore the CN Orange Book registration is directed to the medical use in Swiss-type claim containing such specific crystal form. Therefore, for China, it is important to include at least one composition or medical use Swiss-type claim for drug crystal form patent.

According to the above, Hansoh chose to challenge the patents directed to specific formulations comprising the API dapagliflozin propylene glycol hydrate, and the medical use of the crystalline API. Comparing with the chemical compound patent CN200910158686.6 (which Hansoh chose to deal with using a type 3 declaration), there is higher chance to get around these formulation and medical use patents, for example by not using dapagliflozin propylene glycol hydrate, but uses dapagliflozin itself (whether this would be caught by equivalence is another question). In fact, Hansoh declared that the API in their generic drug is different from that in these 3 CN patents, i.e. dapagliflozin propylene glycol hydrate.

AstraZeneca had until 6 September 2021 (45 days from 23 July 2021) to file a complaint against Hansoh's type 4.2 declaration against the 3 CN patents above at the Beijing IP Court, or at the CNIPA. Failure to do so would result in that the drug marketing approval application would be processed as normal by the China National Medical Products Administration as usual, i.e. without any delay.

If AstraZeneca filed the complaint and was accepted (by the Beijing IP Court, or the CNIPA), and a decision was made within 9 months from the date of acceptance of the complaint:

- if the decision was in favor of AstraZeneca, the drug marketing approval would be delayed to shortly before the expiry of the above three patents, i.e. maximum delay up to 2028.
- if the decision was not in favor of AstraZeneca or not within 9 months, the drug marketing approval would be processed as normal with no delay.

However, as Hanosh undertakes a type 3 declaration against CN200910158686.6, the earliest date that Hanosh could put their generic drug on the market in China is 15 May 2023.

Drug patent linkage complaint situation in China in Dec 2021

For the first type 4.2 declaration discussed above, I have tried to check whether AstraZeneca had filed the complaint at the Beijing IP Court the CNIPA by 6 September 2021, but no luck. In light of the relative ease of getting around the above three subject patents, and Hansoh undertakes that they would only put their drug onto the market after 15 May 2023, AstraZeneca may choose not to file the complaint against the type 4.2 declarations.

On the other hand, according to the announcements from the CNIPA and the Beijing IP Court at the respective links below, 12 drug patent linkage complaints (out of 23 filed) have been accepted by the CNIPA as of October 2021, while 1 has been accepted by the Beijing IP Court as of November 2021 (not clear how many were filed at the Beijing IP Court and were rejected).

- https://www.cnipa.gov.cn/art/2021/10/29/art_53_171065.html
- <https://mp.weixin.qq.com/s/0PNtsF0XBuwxULgYqnV-Uw>

The CNIPA did not provide any details on the complaints they accepted, but the Beijing IP Court did. Specifically, the drug at issue of the complaint accepted by the Beijing IP Court is Eldecalcitol of the Japanese company Chugai Pharmaceutical Co., Ltd. (under the brand Ediol) for treating osteoporosis. The generic supplier is Wenzhou Haihe Pharmaceutical Industry. The patent at issue is CN ZL2005800098777.6.

Apparently the CNIPA has accepted more cases than the BJ IP Court. After checking with the CNIPA, the reason appears to be that the CNIPA does **NOT** require notarization and legalization of formality documents including the Power of Attorney and the business registration certificates to accept the complaints. Specifically, the CNIPA only requires Power of Attorney with a simple signature, while only notarization is required for the business registration certificates, to accept the complaint.

By contrast, the BJ IP Court requires notarization **AND** legalization of the above formality documents in order to accept the complaint. Practically, it is very difficult, if at all possible, to fulfil these requirements within 45 days, especially during the current pandemic.

Such discrepancies on handling of formality documents are reflected on the differences in the numbers of cases accepted (CNIPA 12, BJ IP Court 1).

If the CNIPA continues with this practice, such could make CNIPA a more preferable forum for filing drug patent linkage complaints than the Beijing IP Court. This is because a drug patent linkage complaint must be filed within 45 days from the date of announcement of the relevant 4.2 declaration, otherwise there would be no delay on the drug marketing approval process at the NMPA, i.e. as drug patent linkage protection does not exist. Therefore, the CNIPA is the only choice after the complaint is rejected by the BJ IP Court.

Assuming that the CNIPA made the announcement shortly after they accepted the first drug patent linkage complaint, if a decision was made on the first case by July 2022 and found the generic drug to fall within the scope of the patent, then the NMPA should stop the drug marketing approval process until 20 days before the patent expired. Otherwise, the drug marketing approval process would proceed as usual.

Drug patent linkage complaint situation in China in June 2022

In April 2022, both Beijing IP Court and the CNIPA have announced that they have made their respective first drug patent linkage decision, with Beijing IP Court made the first announcement on 15 April 2022, and the CNIPA followed suit on 25 April 2022 at the links below (looks like the Beijing IP Court and the CNIPA were competing to announce):

- Beijing IP Court - <https://mp.weixin.qq.com/s/-9SocP2TLE20Xw7me3OxNw>
- CNIPA - https://www.cnipa.gov.cn/art/2022/4/25/art_53_175126.html

Both decisions ruled in favor of the generic supplier. While there were critics that these are yet another examples that China is not protecting intellectual property properly, the patents relied on by the DMAH appear to be able to be get around relatively easily, resulting in these decisions. Details of these cases will be discussed below.

Beijing IP Court first drug patent linkage decision (the Eldecalcitol case)

Details of the case are as below:

- The drug at issue is Eldecalcitol of the Japanese company Chugai Pharmaceutical Co., Ltd. (under the brand Ediol) for treating osteoporosis.
- The generic supplier is Wenzhou Haihe Pharmaceutical Industry (Haihe).
- The patent at issue is CN ZL2005800098777.6 ('777).

As mentioned above, Haihe was found by the Court to be not falling within the scope of '777 literally or by equivalence, for which claim 1 specifies the following:

- The degradation of the active ingredient ((5Z,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol) into specific degradation products (6E-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5(10),6,8(9)-triene-1,3,25-triol and/or (5E,7E)-(1R,2R,3R)-2-(3-hydroxypropoxy)-9,10-secocholesta-5,7,10(19)-triene-1,3,25-triol) is suppressed.
- After being stored for 12 months at room temperature and shading, the amount of the degradation product is 1% or less.

It may not be that difficult for the generic of Haihe to get around claim 1 of '777. For example, this could be achieved by showing that the degradation product of the generic is significantly more than 1% after being stored for 12 months at room temperature and shading.

The announcement also mentioned that the patentee Chugai is going to appeal the decision, which resulted in the CN Supreme Court final decision issued on 5 August 2022, which is outside the 9-months window to suspend the DMA process of Haihe at the NMPA. Further facts in the Beijing IP Court decision were revealed in the appeal decision, which will be discussed further below.

It is worth noting that the Beijing IP Court's announcement specifically recited "allowing Chinese people to have good and cheap drugs". This may reflect the attitude of the Chinese government and the courts on the purpose of the Chinese drug patent linkage system, which does not seem to be too encouraging to original drug developers. On the other hand, as the generic may have tried to avoid the scope of '777 by proving to have more degradation product after 12-months of storage, it is curious to see how such could be qualified as "good" drugs.

CNIPA "first" drug patent linkage decision (the oxycodone case)

The drug at issue is oxycodone hydrochloride sustained-release tablets to relieve severe pain (like those because of cancer) of Purdue Pharma under the brand OxyContin (basically, an opioid painkiller). The generic applicant is Yichang Renfu Pharmaceutical Industry Limited Liability Company (Renfu, 宜昌人福药业有限责任公司).

The patents at issue are 201210135209.X, 201510599477.0, and 201010151552.4.

201210135209.X and 201510599477.0 belong to the same family of WO/2008/023261A1 with priority from US60/840,244, and therefore also have the same filing date of 24 August 2007 and full term expiry of 24 August 2027.

201010151552.4 belongs to a different family of WO/2005/097801A1, with full term expiry on 30 March 2025.

As mentioned above, the CNIPA ruled that the generic drug from Renfu does not fall with the scope of the patents at issue.

Renfu also challenged that the recordal of 201010151552.4 (in the drug patent database at NMPA) is incorrect, but this challenge was not recognized by the CNIPA, while the reason is not specified in the CNIPA's announcement above.

The main claims of 201210135209.X, 201510599477.0, and 201010151552.4 could be summarized as below, in addition to the active ingredient oxycodone hydrochloride:

CN patent	Requirements in main claim
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201210135209.X	at least one polyethylene oxide having, based on rheological measurements, an approximate molecular weight of at least 1,000,000, of at least 80wt% of the composition
201510599477.0	at least one polyethylene oxide having, based on rheological measurements, an approximate molecular weight of at least 800,000, of at least 80wt% of the composition
201010151552.4	Limits the amount of 14-hydroxycodeinone, an undesirable precursor of oxycodone, to be less than 15ppm in the composition

Again, it may not be that difficult for the generic of Renfu to get around the claims of the above 3 three patents. For example, this could be achieved by not using polyethylene oxide at all or using another component that does not literally or by equivalence fall within the scope, and showing that the undesirable precursor 14-hydroxycodeinone presents in an amount of more than 15ppm in the composition.

Observations from CN drug patent linkage decisions as of June 2022

It is interesting to see that the challenges from the generics in China thus far (the above challenge from Renfu, the challenge from Haihe in the BJ IP Court decision, and the first type 4.2 declaration from Hansoh) all refer to generics having seemingly properties inferior to the respective original drugs, while from the Beijing IP Court announcement that the purpose of the CN drug patent linkage system is to provide good and cheap drugs for people in China according to the BJ IP Court decision (My head is spinning to understand how drugs having more degradation product or undesirable precursor could be good drugs).

Another point to note is that the CNIPA's announcement above on 25 April 2022 also mentioned that 39 drug patent linkage complaints have been accepted out of 59 filed thus far, a significant increase from the previous CNIPA's announcement in October 2021 (12 accepted out of 23 filed). This shows that the CNIPA is indeed becoming the more favorable forum for drug patent linkage disputes.

Current drug patent linkage complaint situation in China in November 2022

The most significant incident is that the CN Supreme Court issued the first CN drug patent linkage final decision after appeal, which was the appeal against the first CN drug patent linkage decision at the Beijing IP Court mentioned above, the Eldecalcitol case, on 5 August 2022.

This Aug 2022 appeal decision also revealed some facts in the first Beijing IP Court (BJ IP Court) decision, which will also be discussed below.

Firstly, the following was revealed in the appeal decision:

- 15 Apr 2021 and 10 June 2021, two invalidation petitions were filed by two different Sichuan drug companies, respectively, with essentially the same invalidation grounds.
- 2 July 2021, Chugai amended independent claim 1 to incorporate part of subject matter of claim 2, specifically limiting the antioxidant to be dl- α -tocopherol, to address issues raised in invalidation proceedings.
- 16 August 16 2021, Haihe submitted its 4.2 declaration that its generics would not infringe original claim 2 (which was still broader than claim 1 amended by Chugai on 2 July 2021).
- 30 December 2021, CNIPA issued its invalidation decision, invalidating all claims of '777.
- 15 April 2022, BJ IP Court issued its first instance decision.

The appeal decision maintained the BJ IP Court decision that the generic did not infringe literally or by equivalence, there are the following main points:

Details on the first decision at the BJ IP Court revealed in the Aug 2022 final decision

- 1) In this first decision in April 2022, specifically before the deadline to file the drug patent linkage complaint, the subject patent CN ZL2005800098777.6 ('777, for the drug under the brand Edirol) of the patentee Chugai Pharmaceutical Co., Ltd. (Chugai, a Japanese pharmaceutical company) has been announced to be invalid by the CNIPA in December 2021. This invalidation decision itself is under appeal, and therefore the BJ IP Court continued with this case.
- 2) During the invalidation process, it appeared that Chugai amended independent claim 1, the only independent claim in '777, to specify that the antioxidant in the composition is dl- α -tocopherol, and such is used as the basis in this first decision at the BJ IP Court.
- 3) During this first instance decision, the generic supplier Haihe declared that the antioxidant Haihe used was not dl- α -tocopherol, but one of the antioxidants "tocopherol acetate, dibutylhydroxytoluene, natural vitamin E, dl- α -tocopherol, concentrated mixed tocopherol, ascorbyl palmitate, L-ascorbyl stearate,

butylhydroxyanisole, and propyl gallate” except dl- α -tocopherol recited in paragraph [0029] of the Chinese description (see paragraph [0025] of the corresponding EP1714656A1) [Note: the identity of the exact antioxidant was redacted in the link].

4) Chugai then argued for infringement by equivalence, which was refused by the BJ IP Court on the basis that Haihe’s antioxidant has been recited in the description of ‘777 but not chosen by Chugai when amending claim 1 at the invalidation proceeding, and therefore has been surrendered by Chugai (according to Article 5 of the Court’s patent infringement disputes explanations), although Chugai argued as below:

- Article 5 applies to claims before amendments, or at least should include claims before amendments (it is not clear what Chugai intended this “before amendments” to mean, i.e. before any amendments to the claims during prosecution, or before amendments during invalidation). The BJ IP Court decided that this cannot be the case, or otherwise there would be two claims in force *ab initio*.
- Article 5 should apply only when there is intention from the patentee to surrender, which the BJ IP Court decided to be irrelevant.

Details of the Aug 2022 appeal decision at the Supreme Court

In this Aug 2022 appeal decision, it was revealed that the 4.2 declaration Haihe filed at the NMPA was directed only to original claim 2 of ‘777 as below:

2. The preparation according to claim 1, wherein the antioxidant is one member selected from dl- α -tocopherol, dibutylhydroxytoluene, butylhydroxyanisole, and propyl gallate.

This claim 2 was broader than Chugai’s claim 1 after amendments at the invalidation proceeding, which limits the antioxidant to be only dl- α -tocopherol.

Haihe tried to change their 4.2 declaration at the NMPA on 9 December 2021 to direct to claims 1-7, but was refused by the NMPA.

In the appeal, Chugai requested the Supreme Court to order the following investigation reports to show that Haihe violated the NMPA’s requirements when applying for their generic drug marketing approval, and to prove infringement:

l) Report 1 to show that among the non-infringing antioxidant used by Haihe and dl- α -tocopherol, dl- α -tocopherol is the only one legally allowed by the NMPA, and therefore

Chugai believed that Haihe replaced the non-infringing antioxidant by the infringing dl- α -tocopherol

- II) Report 2 to show that Haihe did not declare what antioxidant was used when applying for the generic drug marketing approval. Haihe only provided such information when Chugai filed the drug patent linkage complaint the Beijing IP Court.

Based on the above, the Supreme Court ruled on the following points:

1. Correspondence between the 4.2 declaration with the patent claim

The Supreme Court ruled that the BJ IP Court was correct to use the claims after amendments at the invalidation to rule.

The Supreme Court was unhappy with the “hide and duck” attitude of Haihe when applying for generic marking approval at the NMPA, especially that Haihe only notified Chugai the antioxidant Haihe used after Chugai filed the drug patent linkage at the BJ IP Court. The Supreme Court stated that the BJ IP Court should point this out and criticize this in their decision. However, Supreme Court stated this was not part of the remedy, and therefore would not affect the final decision.

2. What antioxidant actually used by Haihe

According to the declaration submitted by Haihe to the NMPA, the antioxidant Haihe used was indeed not dl- α -tocopherol. The Supreme Court also stated that what is actually used by Haihe was not an issue this case. This case was to determine whether the drug according to Haihe’s declaration to NMPA fell under the scope of Chugai’s patent. It is NMPA’s business to determine whether this Haihe’s antioxidant is legally allowed.

Chugai’s request for the two investigation reports were also denied by the Supreme Court.

3. Whether Haihe antioxidant infringed Chugai’s patent by equivalence

In addition to surrender, the Supreme Court also ruled on this point using estoppel, albeit Chugai argued that their amendment to recite dl- α -tocopherol as the only antioxidant was due to support allegations. The Supreme Court specifically stated that Chugai did not provide any reasons or evidence showing that Chugai did not abandon the other

antioxidants by amending the claims during invalidation. [Note: This is catch-22. If Chugai could do so, why would they amend to keep '777 in force?]

Observations from this first CN drug patent linkage final decisions of Aug 2022

The mechanism of the current CN drug patent linkage declaration and notification is defective, but is understandable as the system is still at its early stage. Specifically, the system should require that the generic notifies the drug patentee of the complete composition of the generic drug, including the identify and the amount of all ingredients, at least when filing the type 4.2 declaration.

Further, whether the generic is allowed to choose what specific claim in a drug patent to file their type 4.2 declaration is subject to debate. I find it is absurd to do so if the generic is allowed to target one dependent claim as in this case – would this be equivalent that the generic also files a type 3 declaration for the main independent claim, which in this case Haihe did not appear to do so? As such, I suggest if type 4.2 declaration is to be filed by a generic, the generic is at least required to file this 4.2 declaration directed to all of the independent claims. Dependent claims could be chosen, as the generic may not be using components/amounts specified in the dependent claims.

As always, amendments, particularly during invalidation, would have consequences. Integers recited in the description but not included in the claims after amendments would be excluded for infringement consideration easily in China.

The Chinese courts appear to rule on such cases purely from the angle of “pseud-infringement”, i.e. whether the generic drug according to the generic declaration to NMPA falls within the scope of the drug patent, survived after invalidation. Say yes to bifurcation. One point I find interesting is that, after the subject patent '777 was declared to be totally invalid on 30 December 2021, the BJ IP Court still proceeded to issue the first instance decision on 15 Apr 2022. Would the reason be the BJ IP Court wants to be the first to issue a patent linkage dispute decision? This is not a very difficult to decide with not much adverse consequence to the court after all.

As Haihe was not the invalidation petitioner, Haihe should not have known the amendments made by Chugai at the invalidation proceedings (whether the two

invalidation petitioners informed Haihe, who knows?) before filing their type 4.2 declaration. In any event, Chugai's options to amend the claims after grant are very limited, typically limited to incorporating limitations in existing already granted claims. Presenting two amendment options is not welcomed by the CNIPA at any stage.

My view is that, the current system has not considered all the concurrent "wars" (parallel invalidation proceedings, in particular) going on that do not necessarily involve the generic who files the type 4.2 declaration.

According to information I heard (just hear-say), out of 13 decisions made by the CNIPA, half of them is in favor to the DMAH. Unfortunately, these decisions are not available to the public, seemingly under appeal.

Comparison between the US and CN drug patent linkage system

Thanks to the suggestion from Carol Nielsen of Nielsen IP, and review and comments by Corey Salsberg of Novartis, the appendix of this guide has a table showing the differences between the US and China drug patent linkage system.

Conclusion

While the "CN Orange Book" is based on the US Orange Book (as required under the US-CN Phase-I Trade Agreements 2020), the Chinese system has the following characteristics:

- a) The patent information in the Chinese system is much more extensive than that of the US.
- b) There is no drug data exclusivity information in the Chinese system.
- c) Action could only be taken against type 4.2 declaration (the generic drug does not fall within the scope of the patent(s)) in China.

Regarding c), this may be the substantive difference of the CN system from the US system. In essence, in China, there is nothing the DMAH could do to delay the drug marketing approval process at the NMPA if the generic drug applicant simply alleges that the patent at issue should be declared invalid, and does not even challenge the validity of the patent afterwards.

There have been many changes on the “CN Orange Book” since its establishment on 29 June 2021. For example, in the very beginning, the platform did not have different tabs for entries of chemical drug, biological drug, and Chinese medicine. Now individual tabs are available, making searching and counting much easier. Finally, all five types (types 1-3, 4.1, and 4.2) declarations have been announced.

If you are an innovative drug owner, I am not surprised that you have already registered your drug patent information on the “CN Orange Book” to deter generic drug marketing approval application.

For others, including myself heavily involved in drug freedom-to-operate work, the “CN Orange Book” is a mountain full of treasures. Once the Chinese drug name is known (hint: have a look at the drug innovator’s Chinese website), the grant patent publication, claim(s) and subject matter(s) relevant (with clear indication on what claim is covering which subject matter), full term expiry, and invalidation information (if available) are all available in one place.

After the first batch of drug patent linkage complaints have been accepted by the CNIPA and the Beijing IP Court at least in October 2021, while the two decisions thus far could be made within the required 9-months window, these two decisions only favored the generics. However, there may be legitimate reasons for these two decisions, as the patents relied on by the DMAHs in these decisions may not be too difficult to get around. By contrast, as shown in the first 4.2 declaration, the generic specifically avoided the relative strong patent directed to the chemical structure of the active ingredient of the drug.

Generics are apparently trying their best to game the current CN system, but the CN Supreme Court has spotted this. This may result in the NPMA/CNIPA revising the CN drug patent linkage regulations in the future.

Another point to note is that while the Chinese government has the intention that the CN drug patent linkage system is to provide Chinese people with good and cheap drugs, the Chinese generics that have challenged the DMAH do not appear to produce drugs as good as the corresponding original versions.

Appendix - Differences between the US and China drug patent linkage systems

Chemical drug

Aspect	US	CN
New drug exclusivity	5 years	None
Types of declarations	<p>4 types of declarations</p> <ol style="list-style-type: none"> 1. That there is no patent information registered related to the drug. 2. That the patent(s) has already expired, or been declared invalid. 3. The date on which the patent(s) will expire, and that generic applicant promises that the generic drug will not go on the market until the expiry of the patent(s). 4. That the patent(s) is not infringed, or should be declared invalid. 	<p>4 types of declarations as the US, but <u>type 4 declaration</u> is further subdivided into the following types 4.1 and 4.2 declarations:</p> <ul style="list-style-type: none"> • 4.1. the patent should be declared invalid • 4.2. the generic drug does not fall within the scope of the patent
Notification to DMAH	Generic drug applicant to notify the drug marketing approval holder (DMAH) of the type 4 declaration within 20 days after receiving FDA's acknowledgment that the Abbreviated New Drug Application (ANDA) has been received and is ready for substantive review.	DMAH to find out announcement of notice of type 4 declaration from the CN drug patent linkage platform.
Filing of drug patent linkage complaint	DMAH to file suit at a court within 45 days after receipt of notice from the generic drug applicant.	<p>DMAH to file complaint at the Beijing IP Court or the CNIPA with 45 days after announcement of notice of type 4 declaration, but <u>ONLY</u> for type 4.2 declaration.</p> <p>That is, there is no delay of the drug marketing approval process if a type 4.1 declaration is filed.</p>

Stay of generic drug marketing approval process after filing the drug patent linkage complaint	After filing of the suit, the DMAH has an automatic 30-month stay of regulatory approval of the ANDA (which begins on “the later date of receipt” of the notice letter (sent by the generic drug applicant) by the DMAH.	After acceptance of the complaint, and <u>if and only if</u> a decision was made within 9 months from the date of acceptance of the complaint that the generic drug falls within the scope of the patent, the NMPA would initiate the drug marketing approval process 20 days before the patent(s) expired. Otherwise, the marketing approval process would proceed as normal, i.e., as if drug patent linkage protection does <u>not</u> exist.
Types of patents that could be registered	<ul style="list-style-type: none"> • The drug substance (active ingredient), <u>including different crystal forms</u> • The drug product (formulation and composition) • Medical use 	<ul style="list-style-type: none"> • The drug substance (active ingredient), <u>excluding different crystal forms</u> [Note: However, composition patent including the different crystal forms could be registered] • The drug product (formulation and composition) • Medical use
Information contained in the drug patent database	Only US patent numbers and the full-term expiry date are listed.	<p>Extensive information is listed in the drug patent database as below:</p> <ol style="list-style-type: none"> 1) The granted patent itself is available for downloading at a link on the same page. 2) The claim number(s), and the relevant subject matter, are clearly identified. 3) The full-term expiry of the patent(s) is clearly identified. 4) Whether the patent has survived through invalidation is also specified in the note section.

Incentive to generic drug applicant	180 days marketing exclusivity to the first applicant to file the ANDA.	12-months exclusivity period to the first successful challenger who files a type 4.1 declaration and subsequently invalidates the patent successfully.
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Biological drug

Aspect	US	CN
Biologic exclusivity	12 years of total market protection, including 4 years before a biosimilar application may be submitted to the FDA, and another additional 8 additional the application may be approved.	None.
Stay of generic drug marketing approval process	None	None.
Types of patents that could be registered	Any patents identified by the reference product sponsor to a biosimilar applicant during the “patent dance”, in which the reference product sponsor and the biosimilar applicant exchange information of patents that may be infringed, and may include multiple waves of litigation.	<ul style="list-style-type: none">• Sequence structure of the active ingredient• Medical use
Incentive to generic biologic applicant	12 to 42 months for “interchangeable biosimilars” (with more information and data available showing the impact of switching such that the intervention of the health care professional is not required, with the first approved by the FDA on 28 July 2021), depending on whether infringement suit is filed, and if filed, the duration of the infringement suit	None.