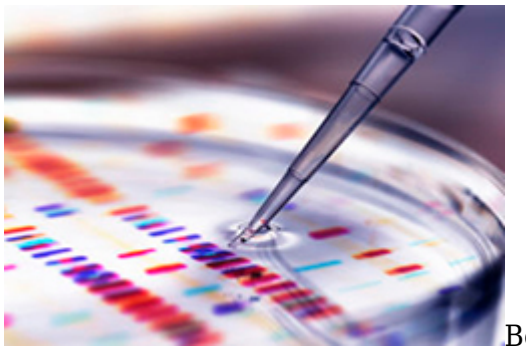
Clinical Holds: Tips for Handling FDA's Call and What to Do Next

 Because life sciences companies hope to never end up on clinical hold, preparing for such a call from the U.S. Food and Drug Administration (FDA) is often not on the to-do list. But there can be significant advantages to advance preparation. Our Goodwin Insight shares some tips for life sciences companies on navigating that first call with FDA and the actions that follow.

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Developing Medical Products for Public Health Emergencies

 The 2019 novel coronavirus (coined COVID-19 by the World Health Organization) is the latest in a series of public health emergencies in recent years to challenge product developers in the life sciences community. With every challenge comes an opportunity, in this case to leverage product development plans and technologies to be first-to-market with products useful in remediating some aspect of COVID-19 and its spread. Earlier this year, the U.S. Food and Drug Administration (FDA) announced its commitment to extend all available resources to help expedite the development and availability of medical countermeasures (MCMs) to prevent, treat, or diagnose COVID-19 and, in fact, issued the first emergency use authorization (EUA) shortly thereafter. For life sciences companies exploring potential opportunities to leverage their programs to help treat, detect, or address some aspect of COVID-19, a number of regulatory mechanisms may be available to facilitate and advance product development plans.

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Q&A on FDA's Requirements Related to Financial Disclosure by Clinical Investigators

What financial arrangements between clinical trial sponsors and clinical investigators must be disclosed in a drug, biologic or device marketing application?

In a marketing application, FDA requires that four types of financial arrangements be disclosed: (1) any financial arrangement between the sponsor and the investigator whereby the value of the compensation to the investigator for conducting the study could be influenced by the outcome of the study; (2) any significant payments of other sorts from the sponsor, such as a grant to fund ongoing research, compensation in the form of equipment, a retainer for ongoing consultation, or honoraria, which are greater than $25,000 in cumulative value and given to the investigator or the investigator's institution to support the investigator's activities, exclusive of the costs of conducting the study, for the duration of the study and for one year following the study's completion; (3) any proprietary interest in the tested product held by the investigator; and (4) any significant equity interest in the sponsor held by the investigator, which is any amount for a non-publicly traded company or an equity interest in a public company valued over $50,000 for the duration of the study and for one year following the study's completion.

How is a clinical investigator defined in the context of FDA financial disclosure regulations?

In FDA's financial disclosure regulations, the agency defines a clinical investigator as a listed or identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

What does FDA look for with regard to financial interest?

FDA looks at several factors with regard to financial interest, including the size and nature of the disclosed financial interest, the steps taken to minimize the potential for bias, and the study design. For example, FDA will evaluate whether the study has been designed with multiple investigators (most without a disclosable interest), blinding, objective endpoints, or measurement of endpoints by someone other than the investigator. FDA may initiate audits of the data from the investigator at issue, request that the applicant submit further analyses of the data or conduct additional independent studies to confirm the results. The agency could also refuse to treat the study as providing data that can be the basis for an agency action. We recommend you contact your Goodwin life sciences or FDA lawyer for further explanation of the agency's financial disclosure regulations.

What has contributed to the rising cost of Directors and Officers (D&O) Liability Insurance for new public companies?

Over the past year, the cost of obtaining D&O insurance for new public companies has increased substantially. Rates have increased from $50-60,000 per million dollars of coverage to over $150,000 per million dollars of coverage. Along with increased premiums, retention amounts have increased substantially (from $5 million to $10 million for smaller public companies up to $30 million for very large public companies). The increased cost of D&O insurance has been driven by the record level of securities class action filings over the last three years, as well as the increased settlement value of such actions (44% higher average settlement value in 2018 than the average of the past nine years according to Cornerstone Research). Further contributing to the increased cost is the U.S. Supreme Court's ruling in the 2018 case, *Cyan, Inc. v. Beaver County Employees Retirement Fund*, that state courts can hear securities claims under the Securities Act of 1933, creating additional uncertainty regarding the outcomes of such cases. These factors in turn have caused some carriers to limit (or entirely eliminate) underwriting D&O insurance for new public companies.

Given that securities class action suits are filed against companies in the life science industry more than any other industry, life sciences companies have been especially impacted by the increased cost of D&O insurance premiums, with rates continuing to rise materially on a monthly basis. One oncology company was given an initial premium estimate of $2.3 million for a June 2019 IPO closing, but ended up paying a premium of $4.3 million when its IPO closed in September 2019. Given these changes in the D&O insurance marketplace, we recommend that companies engage a D&O insurance broker early on in the IPO process to ensure that they will be able to obtain competitive and comprehensive coverage and to avoid last minute surprises when their boards of directors are being asked to approve such high-cost packages. We recommend you contact your Goodwin life sciences or corporate lawyer for further guidance on obtaining D&O insurance.

When does my patent expire?

To determine when your (or your competitor's) patent expires, first identify the correct filing date of the patent application. A U.S. utility patent (filed on or after June 8, 1995) expires 20 years from the earliest filing date of the patent. If the patent claims priority to an earlier patent application, then the 20 year term starts from the filing date of the earlier patent application. (Note, some earlier patent applications are excluded from this consideration and do not impact the patent term). You can determine if your patent claims priority to an earlier patent application by looking at the first page of the patent for a subsection titled "Related U.S. Application Data." Sometimes this information is also found in the first paragraph of the specification of the patent. If your patent claims priority to one or more earlier-filed patent applications, those patent applications will be listed by their application number and filing date in this subsection. Application numbers can be in the format of an international patent application (having the application serial number format of PCT/XXYEAR/######) or in the format of a U.S. patent application (having the application number format of 01/###,### through 16/###,###). Identify the earliest filing date from these patent applications, and the patent term expires 20 years from this date.

However, if the "Related U.S. Application Data" lists one or more provisional U.S. patent applications (having the application serial number format of 60/###,### through 63/###,###), then these filing dates are not used to calculate patent term. If only provisional U.S. patent applications are listed in the "Related U.S. Application Data" subsection, or if this subsection is missing from the front of the patent, then the filing date for purposes of calculating patent term is the filing date listed on the left front page of the patent, indicated as "Filed:" In this case, the patent term expires 20 years from the filing date on the front page of the patent.

In some cases, a patent may be extended beyond its 20 year term. For example, some patents are awarded a patent term adjustment (PTA) by the United States Patent Office. If a patent is awarded PTA, this is typically listed on the front page of the patent. For example, the front of the patent may state, "Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 246 days." If the patent has this award, add the number of days of PTA to the patent term. Additionally, some patents are awarded a patent term extension (PTE) by the United States Patent Office. If a patent is awarded a PTE, a Patent Term Extension Certificate is filed in the file history of the patent. The file history of the patent can be found at **https://portal.uspto.gov/pair/PublicPair**. If the patent has been awarded a PTE, add the number of days of PTE to the term of the patent in addition to any PTA award.

Finally, a patent term may be shortened. In these cases, the front of a patent may (or may not) state that "This patent is subject to a disclaimer." In this case, the patentee has surrendered any patent term (including any PTA) beyond the expiration date of another patent. Identifying this patent or application can be found by reviewing the file history of the patent at **https://portal.uspto.gov/pair/PublicPair**. We recommend you contact your Goodwin life sciences or patent lawyer for a determination of how this disclaimer impacts patent term.

I want to engage a consultant to provide services on behalf of the company, but that consultant is a professor at an academic institution. Can I still do so?

 Yes. Many life sciences and biotech clients work with consultants that are associated with academic or research institutions. However, in considering whether to engage such a consultant, life sciences companies should be aware that the consultant will be subject to the intellectual property and conflict of interest policies of the associated institution. Most (if not all) academic or research institutions require their employees to assign ownership to the institution of any intellectual property (whether patentable or not) created by the employee either (1) in furtherance of the employee's responsibilities for the institution or (2) using university resources (e.g., labspace, funding, laptops, etc.).

When engaging a potential consultant associated with an institution, the institution will need to review the underlying consulting agreement before the consultant signs it. Be sure to build in time for this review. Usually the institutions will look to ensure the consulting agreement includes a reference to the university policies and an acknowledgement that the consultant is subject to those policies while providing services for the company.

After the consultant is engaged following completion of the institution's review of the consulting agreement, the consultant should ensure that any services provided for the company as a consultant are separated from any of his/her responsibilities for the institution or resources provided by the institution. This includes laptops, computers, iPads or other devices. Life sciences companies should ensure this separation is strictly adhered to. Otherwise, there is the potential for the institution to claim ownership over intellectual property created by the consultant, even if it was for or on behalf of the company.

There are certainly exceptions to institutional policies, so the above are not hard and fast rules. We would recommend always connecting with your Goodwin licensing or commercial counsel and discussing directly with the potential consultant and institution in each instance.

I want to license technology out of an academic or research institution. What kind of compensation will the institution typically look to receive?

Academic or research institutions are at the core of early-stage innovation in the life sciences and biopharmaceutical industries. In order to gain access to the intellectual property generated or owned by those institutions, institutions typically offer to grant a license to its owned intellectual property to companies. In exchange for the license, institutions will look for consideration, which comes in a variety of forms. We can break down types of typical consideration into a few categories.

1. License Issue Fee: Institutions may ask for an upfront fee for the grant of the license. This is a one-time payment paid at the signing of the license.
2. Minimum Annual Royalties/Annual License Fees: Aside from the upfront fee, many institutions will ask for an annual "maintenance" fee. These can take the form of yearly lump sum payments, but can also sometimes be called "minimum annual royalties". If these payments are considered minimum annual royalties, then the yearly fee is creditable against any royalties owed to the institution that year.
3. Royalties: Institutions may ask for a percentage of the future sales of products that incorporate the intellectual property licensed. This comes in the form of on-going royalty payments. Typically, for most institutions, these are in the single-digits, but depend on the scope and breadth of the license.
4. Development/Commercial Milestones: Institutions may ask for lump sum payments based on the achievement of certain developmental or commercial milestones by the company. For example, if a product that incorporates the intellectual property licensed from the institution receives FDA approval, the institution may ask for a lump sum payment upon such achievement.
5. Sublicensing Income: Institutions like to ask for what we call "sublicense income". Through sublicense income, the institution is entitled to a percentage of the consideration the company receives from a sublicensee, if the company sublicenses the institutions intellectual property to a third party. The percentage varies and usually decreases over time, but is typically in the single-digits to low double-digits.
6. Patent Costs: If the company is taking an exclusive license, the institution will typically want the company to cover the costs of prosecuting any patents being licensed, those both already incurred and to be incurred in the future. In exchange, typically the company will have input in the future prosecution of the patents.
7. Equity: Depending on the relationship of the institution and the company, some institutions may request equity in the company in exchange for the license grant.

The amount and frequency of the above categories will vary from license to license, and will depend on the scope and breadth of the license (e.g., exclusive v. non-exclusive, limited geography v. worldwide, narrow field v. all fields, etc.). There also may be consideration institutions will ask for, other than the above. We recommend connecting with your Goodwin licensing or commercial counsel to discuss what might be typical for the scope of license you intend to enter into.