Requirement for a Pediatric Clinical Investigation

Starting on August 18, 2020, any drug company submitting an original application for a first-to-be approved or licensed cancer drug that:

1. is indicated for an adult cancer; and
2. is directed to a molecular target determined to be substantially relevant to the growth or progression of a pediatric cancer;

must also submit reports on clinical investigation(s) designed to yield clinically meaningful pediatric study data, gathered using age group appropriate formulations, regarding dosing, safety, and preliminary efficacy. The U.S. Food and Drug Administration, or the FDA, intends to use reports data to inform potential pediatric labeling.

The FDA publishes and regularly updates a list of molecular targets substantially relevant to the growth or progression of a pediatric cancer. This current, seven-page list is subdivided into four sections: gene abnormalities; cell lineage; tumor microenvironment and immunotherapy; and others. A recent briefing document from the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee is available online.

Exceptions, Deferrals and Deferral Extensions, and Waivers

Sufficiently Similar Exception

Some exceptions exist to the clinical investigation and reports requirements. For example, if the course of the disease and the effects of the drug are "sufficiently similar" in adult and pediatric cancer patients, it may be acceptable to conclude that pediatric effectiveness can be extrapolated from the adult clinical studies, supplemented with e.g., pharmacokinetic studies in pediatric patients.

Deferrals and Deferral Extensions

The required pediatric studie(s) and associated reports, at the request of the drug candidate sponsor or on initiative of the FDA, can be deferred until a specified date if:

1. the drug candidate is ready for approval or license in adults before the pediatric studie(s) are complete; or
2. pediatric studie(s) should be delayed until additional safety or effectiveness data have been collected in adults; or
3. there is another appropriate reason for the deferral; and

the drug sponsor submits to the FDA: a certification of the reasons for the deferral; the pediatric study plan; evidence that the pediatric studies are being or will be conducted with due diligence at the earliest possible time; and a timeline for completing the pediatric studies. Extensions of the deferral may be granted by the FDA.

Deferrals require submission of annual reports to the FDA on the progress towards conducting the pediatric study(s). And, the FDA will subsequently make public the reported information, and other associated information.

**Full and Partial Waivers**

At the sponsor's request, or on its own initiative, the FDA may grant a full or partial waiver for the pediatric study(s) and reports requirements. Reasons for granting a full or partial waiver include:

1. the necessary pediatric study(s) are impossible or highly impractical;
2. strong evidence suggests that the drug candidate would be unsafe or ineffective;
3. the drug candidate does not represent a meaningful therapeutic benefit over existing pediatric therapies or is not likely to be used in a substantial number of pediatric patients; or
4. a pediatric formulation is not possible.

**Failure to Comply—Non-Compliance Letters and Misbranding**

Failure to comply by either completing the studies, or obtaining a deferral, deferral extension, or full or partial waiver, will initially result in the FDA generating a non-compliance letter. The drug sponsor must respond to the non-compliance letter within 45 days of letter issuance. And, the response will—with appropriate redactions—be made public.

Beyond this, if the drug is approved or licensed, the FDA may consider the approved or licensed drug to be misbranded. However, and importantly, the failure to comply may not serve as a basis to withdraw drug approval or revoke drug license.

**Patent and Clinical Trial Considerations**

As the pediatric clinical investigation(s) and reports may result in labeling changes, it is worth considering filing additional patent application(s) around this clinical trial data. The timing of these application filings, and their ultimate effect on lifecycle management, should also be carefully evaluated. Budgets should be adjusted to anticipate these filings.

The studies and reports may also require allocation of additional resources. And because of potential failure of clinical trial sites to hit recruiting targets, and potential protocol amendment(s) that may accompany the pediatric study(s), sponsors may wish to consider early engagement of pediatric key opinion leaders, including additional clinical trial site(s), planning for additional delays and expenses in the drug's path to market; further engagement with the institutional review board, or IRB, and thinking about associated informed consent issues.

**Conclusion**

Pharmaceutical companies intending to submit an original application for a first-to-be approved or licensed cancer drug that: 1) is indicated for an adult cancer; and 2) is directed to a molecular target determined to be substantially relevant to the growth or progression of a pediatric cancer; should map out their strategy for complying with the law that goes into effect next year in August. Companies should also consider the impact of the law on their budgets, patent application filings, lifecycle management, clinical trial planning, key opinion leader engagement, and path and timeline to market.

For questions regarding pediatric studies and reports, or any related matter, please contact Vern Norviel, David Hoffmeister, Georgia Ravitz, James Ravitz, Lou Lieto, Mike Hostetler, or any member of WSGR's patents and innovation strategies or FDA/life sciences groups.

*Charles Andres contributed to the preparation of this WSGR Alert.*