An evaluation of the minutes of subject expert committee meetings of novel COVID-19 proposals

INTRODUCTION

The Drugs Controller of India seeks the opinion of the Subject Expert Committee (SEC) for applications received and an analysis of their functioning for COVID-19 studies will lend useful insights into the drug development process in the country during the pandemic. This formed the study objective.

METHODS

We analyzed minutes of the SEC meetings on COVID-19 (April 8, 2020–January 31, 2021) and excluded items that were postponed/deferred or were internal discussions. Each item was classified as initial/repeat application; category of the interventional product was classified as repurposed/novel and the therapeutic area was noted down. The purpose of the application was classified as permission to conduct computed tomography [CT]/amendment of approved protocol/Marketing authorization (MA) with CT waiver or MA post-CT.

Categories of the applicants were divided as Indian pharmaceutical companies/foreign multinational companies (MNCs) or Contract Research Organization (CROs). Outcomes were accepted, rejected, or clarification sought. Turnaround time (TAT) was calculated as difference between date of first hearing and date of final decision.

Descriptive statistics were used to summarize quantitative data. Nonnormal continuous data were analyzed using Mann–Whitney U-test. The Chi-squared test was applied to assess the difference in outcomes with regards to the purposes of applications. The overall level of significance was set at 5%. Multiple comparisons (n = 12) were made using post hoc Beasley's technique with Bonferroni's correction and the P value for this was set at 0.004 (P < 0.05/12).

RESULTS

Seventy meetings with n = 352 agenda items were identified. A total of n = 329 items formed the final sample. (241 agenda items and 109 IPs). The median (interquartile range [IQR]; Q1, Q3) number of agenda items per meeting was 5 (4; 3.7). Eighty of 109 (73.4%) were proposals for repurposed agents and n = 28/109 (25.7%) were exclusively developed for COVID-19 and one was medical device application.

Of the repurposed agents, n = 11/80 (13.8%) were CAMs, n = 7/80 (8.7%) were disinfectants and n = 62/80 (77.5%) were drugs from allopathy. Among the allopathic agents, n = 26/62 (41.9%) were drugs, while n = 36/62 (58.1%) were biologics including n = 12 vaccines. Anti-infective agents formed the largest category for repurposing (n = 24/62; 38.7%), followed by cardiology, rheumatology, anti-inflammatory drugs (n = 6/62; 9.7% each), hematology, and oncology (n = 5/62; 8.1% each).

The most reason for the application was permission to conduct a CT (n = 170/241 (70.6%). Applicants were from Indian pharmaceutical industry as also MNCs (n = 134/241 (55.6%). The most common request was to approve the conduct of a phase III CT (n = 41/170; 24.1%) followed by Phase II (n = 32/170; 18.8%).

Most applications that sought permission to conduct CTs (n = 102/170; 60.0%) and to amend an existing protocol (n = 16/22; 72.7%) were approved. One hundred and forty of 241 (58%) applications were accepted and fifty five of 241 (22.8%) were rejected. There was a significantly high number of rejections for applications seeking MA with CT waiver (n = 16/33; =48.5%, P = 0.0001) and a significantly lower number of rejections for applications seeking permission to conduct CT (n = 29/170; 17.1%, P = 0.001) on post hoc analysis.

One hundred and thirty-four of 170 (78.8%) applications were given a decision at the first instance. The overall TAT [Median (IQR; Q1, Q3)] for all approved applications was 1 (11; 1,12) and that for all rejected applications was 1 (0; 1,1) (P = 0.004; level of significance P < 0.05). There was a significant difference in TAT (P = 0.032) between the accepted and rejected applications that sought permission to conduct CT.
DISCUSSION

SEC minutes reflect the nature and extent of drug development in India.[2] The Indian regulator conducted as many as 70 meetings (329 agenda items) over 10 months for COVID-19 alone. A quarter of products were novel while the remainder repurposed. Anti-infectives were commonly repurposed and the median TAT was just one day. Close to 80% applications for conduct of clinical trials were approved at the first instance.

The fact that nearly three-fourths of the IPs were for repurposing shows that this was the best bet given that new drug discovery was simply not possible.[3] The fact that anti-infectives, anti-inflammatory, rheumatology, and cardiology drugs were seen in the applications indicates that drug repositioning was multi-modal.[4] Similar to the earlier study,[5] permission to conduct CT was the most common purpose of the application.

The vast majority of applications that sought permission to conduct CT were approved. Maximum rejections were for applications that sought MA with CT waiver. These findings align with the earlier study.[5] We did not find a significant difference between accepted and rejected applications [median TAT was just 1 day for both] indicating an expeditious decision-making process by the SEC. Our study is limited by the fact that not all variables of interest were present in the SEC minutes. Furthermore, we did have nonCOVID studies as controls. In summary, the Indian regulator conducted a large number of meetings during the pandemic with an expeditious review. This has helped drug development and consequent product approvals for the disease in India.

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Conflicts of interest
There are no conflicts of interest.