INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Extended-Release Opioid Agonists and Antagonist Medications for Addiction Treatment (MAT) in Patients with Opioid Use Disorder

Response to Public Comments on Draft Evidence Report

October 25, 2018

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Manufacturers		
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1.	In the Background section of its Draft Report dated September 7, 2018, ICER states: "Despite the essential role of MAT in treating OUD and in preventing harm, including death, an important gap persists between the need for and the availability of MAT. More than 30 million people live in US counties without a single prescriber for addiction treatment, and even if existing treatment capacity is reached, one million people would still lack access to treatment. Expanding access to OUD medications is considered an important public health strategy for countering the opioid epidemic." Yet despite making these statements, ICER's focus in the Draft Report is not expanding access to these essential medications, but comparing medications that are not approved for the same indication. Alkermes strongly encourages ICER to reframe the policy focus of the Report as how can we improve equitable access to all MAT options for persons suffering from OUD. The current focus has the very real potential of exacerbating the existing problem of access in the middle of an epidemic.	The focus of the report was deemed to be appropriate and has been vetted through the comments received for the scope from stakeholder groups, including clinicians and patient groups.
2.	As recognized by SAMHSA and articulated in the FDA-approved indications, these products are not interchangeable. Patients initiating treatment with BUP-NX are in a very different phase of the disease than the patients who initiate treatment with XR-NTX. In the clinical comparative effectiveness section, ICER acknowledges, "Differences observed between Vivitrol and buprenorphine/naloxone are due at least in part to differences in treatment intent and goals." Further, under the section "Controversies and Uncertainties" at the end of the Comparative Clinical Effectiveness section, ICER states, "As noted by SAMHSA in the 2018 TIP, no evidence clearly predicts which patients are best treated with Vivitrol versus methadone or buprenorphine formulations. The treatment sequences for different subpopulations with OUD cannot be based solely on the available evidence, but rather must be informed by clinical knowledge and the local context." Given these facts acknowledged by ICER itself, it is perplexing why ICER has chosen to compare these very different medications to each other. Again we strongly encourage ICER to reconsider the policy question, not to focus on how these quite distinct medications compare to each other, but rather on how we can	As described in the analytic framework, the report looks at populations with OUD that seek MAT. The analytic framework allows us to provide a coherent comparison of all the different extended-release formulations. As stated in the section on potential other benefits, ICER recognizes that "patients need to have access to different treatment options on their road to recovery" and that "extended-release formulations are important additional treatment options." These benefits will be presented together with the evidence on the clinical and economic dimensions at the public deliberative meeting of the New England CEPAC on November 8, 2018. The resulting policy recommendations may include the dimension of improving access to MAT.

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	improve equitable access to all medications for persons suffering from OUD, so that a person can choose the medication that is most appropriate for him/her at any given point in his/her journey with the disease.	
3.	ICER's conclusions from the comparative clinical section are that XR-NTX has comparable net health benefit to BUP-NX with a high degree of certainty. It is confusing to a reader who is not well versed in CEA that the conclusion from the CEA is that XR-NTX is "less effective and more costly" than BUP-NX. In other words, the conclusions from these two sections are inconsistent. Further, if XR-NTX and BUP-NX are equally effective (as the scientific data suggested [Lee et al., 2018; Tanum, 2017] and ICER concluded), a cost minimization analysis, not a CEA, is most appropriate according to traditional economic methods (Drummond et al., 1997). Finally, the conclusion from the CEA regarding "less effective" is based on inappropriate assumptions (summarized below in "Utility Values").	Vivitrol had a comparable net health benefit to buprenorphine/naloxone specifically in the intent-to-treat efficacy analyses. That language has now been added to the comparative clinical section of the report.
4.	Patient Population. Standard cost-effectiveness analysis states that the target population under study be well-defined and consist of those who would receive the interventions being modeled (Roberts et al., 2012; Drummond et al., 1997). However, in this case the target population for the model is listed as "(P)articipants ages 16 years or older who are seeking detoxification, maintenance treatment, or long term recovery from OUD." Patients seeking "long term recovery from OUD" may seek either detoxification or maintenance treatment; however they typically do not seek them both together. As detailed above, patients seeking detoxification from opioids followed by XR-NTX versus maintenance therapy with an opioid agonist are distinct patient populations as these are very different treatment options. In fact the Surgeon General and SAMHSA recently stated that all patients with OUD who are detoxified from opioids should be offered XR-NTX (US HHS, 2018). These treatments are not substitutable and in fact as described by ICER, "initial pathways differed for each intervention based on trial design and FDA label...." The differences between opioid agonist versus antagonist medications are summarized in detail above. To include these distinct patient populations in the same cohort and consider them eligible for the same medications is contrary to the underlying principles of CEA. Finally with respect to the patient population, we again remind ICER that XR-NTX is only	The target population in the cost-effectiveness analysis includes adults diagnosed with OUD and seeking treatment with MATs. Our objective was to establish the value of different MATs in an OUD population seeking treatment with one of the many MAT treatment options. We acknowledge that each MAT has treatment pre-requisites and these entire "treatment" pathways have been included using the decision tree prior to patients entering the Markov model in the cost-effectiveness analysis.

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	indicated for patients 18 years and older; therefore it is not appropriate to consider 16- and 17 year-olds in an economic model of XR-NTX.	
5.	In CEA, all relevant alternatives for the question under study should be included (Roberts et al., 2012; Drummond et al., 1997). Assuming it is appropriate to compare opioid agonist to opioid antagonist medications, ICER has omitted an important alternative—the one that most patients with OUD are currently receiving—no medication treatment.	We gathered from discussions with several stakeholders that OUD patients are offered one of several MATs and "no treatment" isn't a widely practiced option.
6.	Despite the very limited data available on utility values associated with OUD and its treatment, ICER has elected to estimate a cost-per-quality adjusted life year (QALY) as the only outcome for the CEA. Importantly, ICER does not include a discussion of the significant limitations of this outcome in this disease area, nor does it include any alternative outcomes for the incremental cost-effectiveness ratio (e.g., cost per life-year saved or cost per abstinent day). The conclusions of the CEA with respect to XR-NTX are based on a marginal (0.03) difference in QALYs. However, the single study from which utility values were obtained included health states for persons on buprenorphine and methadone, but not for XR-NTX. The fact that utility values for buprenorphine were used as a proxy for utility values for XR-NTX was never stated in the ICER report; one would have to go to the original data source (Wittenberg et al., 2017) to understand this detail. In Wittenberg et al., the utility values associated with buprenorphine therapy were found to be significantly different from utility values associated with methadone; this is not surprising, as patient preferences are different for these medications (Uebelacker et al., 2016). Furthermore, given the differences between opioid agonist and antagonist medications, we should expect utility values for buprenorphine to differ from those associated with XR-NTX. Yet the ICER model assumes that the utility value associated with being stable on buprenorphine is equal to that of being stable on XR-NTX. This is not an appropriate assumption, and violates what we already know about these medications, i.e., that patients express specific preferences for one versus another at a given point in their disease (Uebelacker et al., 2016). This significant limitation is not discussed in the ICER report, nor did ICER attempt to assess the impact of this limitation on the CEA results by conducting a sensitivity	We have now included language stating that the source of utility estimates was limited to buprenorphine/naloxone, but extended to Vivitrol as well. We'd like to point out that the Wittenberg et al. study used a "direct method" of measuring utilities and the included sample was presented as a "hypothetical" vignette for each described health state. We also conducted sensitivity analyses on the utility values for Vivitrol as well as other MATs and have reported their impact on the model. We are happy to consider any Vivitrol-specific health state utilities in the model if the manufacturer can furnish us with these estimates.

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	analysis on differential utility values. This is not in keeping with good reporting practices in CEA (Drummond et al., 1997).	
7.	Good practice in CEA stipulates that researchers provide allowance for uncertainty and are clear on the extent to which uncertainty affects the results (Caro et al., 2012). The handling of uncertainty in ICER's analysis is minimal at best. As summarized above, one of the critical inputs into the CEA is utility values. However, ICER did not assess results under an alternative, more realistic assumption that patients on buprenorphine and XR-NTX have different health-related quality of life outcomes (i.e., utility values). ICER used data from Shah et al. (2018) to estimate background healthcare costs, however the medication-specific costs from the study were not used. Rather, ICER states, "We calculated the population-weights average costs of inpatient, ED, and outpatient visits among the Vivitrol and buprenorphine treated populations at baseline and follow-up…" ICER used these estimates as background costs for 3 distinct health states. Yet nowhere in the report does it describe that results from Shah et al. indicate that XR-NTX patients experienced no increase in costs while buprenorphine patients experienced a statistically significant 43% increase in costs. ICER did not explore the impact of differential background costs in sensitivity analyses. In fact, the current structure of the economic model does not allow for differential costs and utility values for BUP-NX and XR-NTX to be tested.	We have included additional language on the limitations of using estimates from Shah et al. We'd like to clarify that all health care costs were subjected to sensitivity analyses in our one-way and probabilistic analyses, and the results of these are presented in the report. Additionally, we'd also like to clarify that the structure of the model can handle differential costing.
8.	Furthermore, while ICER conducted a "modified societal perspective," they did not include potentially one of the biggest drivers and differentiators between generic BUP-NX and all of the extended release formulations: the risks and costs associated with diversion, misuse, and abuse. This is a glaring omission, as diversion is of importance to buprenorphine prescribers (Lin et al., 2018) and was one of the reasons extended-release buprenorphine products were developed (Rosenthal et al., 2017). In one study of opioid, polysubstance users seeking treatment in a drug-free residential recovery center, researchers reported that less than 10% of former buprenorphine users obtained it through a medical prescription and over 90% obtained it via illegal means (Walker et al., 2018). Furthermore, over 70% of former buprenorphine users reported that they took other drugs or alcohol to get high while taking it, and over 80% reported selling, trading, or giving away their	We acknowledge that diversion is a key component in OUD. However, there are no robust published estimates on diversion of these drugs. Additionally, when considering diversion, it's key to also consider switching to other opioids and the effects of switching, for which there is no robust published data. We have now included language on this in the limitations section of the cost-effectiveness analysis.

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	prescribed buprenorphine. The omission of the unwanted effects of generic BUP-NX from the ICER Draft Report is glaring and leads to inaccurate and misleading conclusions regarding the extended-release formulations of both agonist and antagonist medications.	
9.	We have noted several inconsistencies and inaccuracies in the ICER Draft Report, and wanted to call attention to one in particular. On Page 23, ICER states that the 2012 AATOD Guidelines for using Vivitrol recommend monitoring and frequent liver function studies…"because Vivitrol carries a black box warning for liver complications…" Vivitrol does not carry a black box warning, and Alkermes requests that ICER correct this false statement in the Final Report.	We have corrected this inaccuracy in the report.
10.	To reiterate all the points above, Alkermes strongly recommends that the Voting Questions be reframed such that the focus is on evaluating whether the evidence is adequate to support increased education, awareness, and access to all MAT options for OUD. Only then can we begin to address the sizable gap that exists between the need and availability of MAT.	The voting questions focus on the comparative clinical effectiveness and economic value of the different extended release formulations. The deliberations at the November 8 New England CEPAC meeting are expected to touch upon access to MAT.
Braeburn		
1.	Two relevant studies were left out of your analysis, and we urge you to include them. The first study is described in the poster entitled, "Transitioning patient from sublingual to injectable weekly and monthly buprenorphine" and can be accessed here: http://www.eventscribe.com/2018/posters/asam//PosterViewMOBILE.asp?PID=134169 and then clicking on the "view poster" bar. This open-label study was designed to evaluate the long-term safety of CAM2038 in both patients who were new to treatment and converting from sublingual buprenorphine (SL BPN). A post-hoc, subgroup analysis of the patients who converted from SL BPN demonstrated that CAM2038 weekly and monthly were associated with high retention throughout the study for subjects that were transitioned from sublingual buprenorphine. This information is relevant to the model when assessing the retention of CAM2038 compared with SL BPN.	Thank you for sharing these studies. Our target population includes patients with OUD seeking treatment with MATs, and not those already on MATs wishing to switch treatments.
2.	The second study can be found here: https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2632987?redirect=true. This study was a randomized, double-blind, controlled study to evaluate the degree and duration of the opioid blocking effects of CAM2038 weekly following administration of	Our target population includes patients seeking treatment for OUD with MATs, but this study focuses on OUD patients not seeking treatment with MATs. In addition, we found required inputs for our model from the key CAM2038 trial versus sublingual buprenorphine/naloxone.

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	intramuscular hydromorphone (6 mg and 18 mg) compared to placebo on subjective opioid effects in patients with opioid use disorder, as measureed by the Drug Liking visual analog scale (VAS). The findings show that CAM2038 weekly 24mg and 32mg produced immediate and sustained opioid blockade. The results support the use of CAM2038 for treatment initiation and stabilization without a need for SL BPN. Studies have shown that a substantial proportion of SL buprenorphine treatment failures occur during the first seven days of treatment, so being able to induct with injectable buprenorphine that is therapeutic with first dose is beneficial. Note: Two articles that discuss the SL BPN retention can be found here: • https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2628995/ • https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1490248/ This information is relevant when assessing and modeling the benefits of CAM2038 and SL BPN.	
3.	One study was included in your assessment; however, a critical finding of the study was omitted. The study can be found here: https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2681061. It was the completed pivotal randomized, double blind phase 3 study in 428 patients with moderate to severe opioid use disorder. Phase 1 encompassed the first 12 weeks of the treatment phase that included flexible dosing with weekly CAM2038 while phase 2 encompassed the second 12 weeks that included flexible dosing with monthly CAM2038 vs daily sublingual buprenorphine/naloxone (SL BPN/NLX). The primary endpoint was the responder rate based upon no evidence of illicit opioid use measured by opioid negative urine samples and self-report at prespecified time points. A key secondary endpoint, which was omitted in your assessment, was the calculation of the cumulative distribution function (CDF) of percent urine samples negative for illicit opioids from week 4 through week 24 of the treatment phases 1 and 2. It is important to note that this endpoint was controlled for multiplicity. The primary endpoint met prespecified criteria for non-inferiority. Analysis of the key secondary outcome of CDF of the proportion of opiate-negative urine samples from week 4 through week 24	Thanks for your comment. We used an endpoint reported in the key trial that showed Week 1-24 opioid negative urine samples with self-report, that was cumulative over the trial period. This endpoint was then converted to a per cycle (four week probability). This endpoint does take into consideration the efficacy of CAM2038 relative to its comparator. While we acknowledge that CAM2038, due to its method of administration, may mitigate the risks of diversion/unintended use or abuse and pediatric exposure, there are no robust data to model this. In addition, when we consider diversion, we should also be considering switching to other opioids, for which we also had no robust published data.

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	demonstrated superiority of CAM2038 vs SL BPN/NLX (see figure C on the "Figures" tab of this workbook). This statistical superiority of SC buprenorphine dosed weekly or monthly over the sublingual formulation is notable and should be taken into consideration when considering relative value of CAM2038. Because CAM2038 is an extended release formulation of buprenorphine administered as a subcutaneous injection given by HCPs only, there are other potential benefits of CAM2038 that are important to consider. HCP administration may mitigate risks related to abuse/misuse/diversion and unintended pediatric exposure. Additionally, its extended release profile provides for sustained therapeutic plasma exposure throughout the weekly or monthly dosing period and thus may improve medication adherence and increase treatment retention. This key secondary endpoint is relevant to the model when assessing that value of CAM2038 compared to sublingual buprenorphine (SL BPN/NLX).	
4.	The issues of SL BPN being subject to misuse, abuse and diversion – and the issues resulting from this – do not seem to be addressed in the draft report. Because CAM2038 is administered by a healthcare professional and is intended to never in the hands of the patient, the risk of misuse, abuse and diversion is mitigated. Some points from the paper which can be found here https://www.ncbi.nlm.nih.gov/pubmed/29693427 include: • Among those with a history of BPN use, one-third of the lifetime SL BPN/NLX group and 40% of the recent BPN/NX group had received SL BPN/NLX by prescription and over 90% of both groups had obtained BPN without a prescription at least once. • Among those who had received prescribed SL BPN/NLX over 80% said they had sold, traded, or given away their prescribed BPN at least once. Please also see SAMHSA diversion data: https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.htm#tab1-97A Note: You have to calculate Misuse (712k) as a percentage of Any Use (2,253k). Dividing Misuse by Any Use yields 32%.	The reference cited refers to a study on the subpopulation of polysubstance users who are not representative of the other types of subpopulations with OUD. A significant part of the diversion is related to self-medication. As outlined in our report, the lack of access to MAT is an important driver of diversion for self-medication, especially in correctional settings. Furthermore, the advantage of reduced diversion is common to all extended-release buprenorphine products, as mentioned in the report.
5.	We urge you to include in the clinical guidelines section the Treatment Improvement Protocol, TIP 63, entitled "Medications for Opioid Use Disorder: For Healthcare	Thank you. We have added TIP 63 to Section 2.

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	and Addiction Professionals, Policymakers, Patients, and Families" instead of older guidelines. It can be found here: https://store.samhsa.gov/shin/content/SMA18-5063FULLDOC/SMA18-5063FULLDOC.pdf.	
Indivior		
1.	Indivior would like to raise the following specific concerns related to ICER's conclusions about SUBLOCADE in the draft evidence report: • The analysis overstates discontinuation and miscalculates the abstinence rate of SUBLOCADE as compared to generic sublingual buprenorphine/naloxone (Generic SL bup/nal). • The framework adopted by ICER does not explicitly include the numerous societal and contextual considerations critical to real-world treatment of patients with OUD such as misuse, diversion, and pediatric exposure.	Thank you for your comments. We have reviewed our methods used in the Sublocade versus sublingual buprenorphine/naloxone analysis and have moved this analysis from the base case to a scenario analysis. This decision was made because we believe there isn't enough published data available to make a comparison of these two MATs that would warrant inclusion in the base case. Concerning misuse, diversion, and pediatric exposure, these outcomes were included in our analytic framework and literature review, but we did not find publications for these outcomes for the extended-release formulations. For diversion, it is important to note that a significant driver of diversion of buprenorphine transmucosal products is related to self-medication, especially in correctional settings. A significant proportion of diversion thus seems to be linked to difficulties in accessing MAT.
2.	Recommendation 1: The model should assume comparable rates of discontinuation between SUBLOCADE and Generic SL bup/nal during the induction and dose adjustment period. The model incorrectly assumes that nearly a quarter of subjects receiving SUBLOCADE in the US-13-0001 study immediately discontinued treatment. As a result, ICER assumes 24.2% of patients enter the model in the health state "off MAT with use of illicit opioids" (Table 4.1)—the equivalent of illicit use without recovery until death (Figure 4.1B). On the other hand, ICER assumes that a far smaller proportion (0.3%) of the cohort treated with Generic SL bup/nal start in the "off MAT with use of illicit opioids" health state. This assumption substantially mitigates SUBLOCADE's projected incremental clinical benefit. The US-13-0001 study included a 14-day "run-in" period prior to initiating treatment with SUBLOCADE to ensure that potential subjects could meet the requirements for participation in the study. As a result, around 25% of potential subjects did not advance to the full study. However, there is no evidence to suggest that subjects who did	Upon further review of the studies included in the network meta-analysis, we decided to include a Sublocade versus buprenorphine/naloxone comparison as a scenario analysis and exclude this comparison form the base case. Given similar dose frequency and route of administration, we assumed Sublocade to have the same efficacy and discontinuation rate as CAM2038. This scenario also assumes the same induction success/failure rate as CAM2038, at almost 100% successful induction. In the CAM2038 versus buprenorphine/naloxone trial, the two interventions had similar discontinuation rates. This scenario is overall favorable to Sublocade.

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	not complete the run-in period for non-medical reasons (e.g., inflexible work schedule or lack of transportation, etc.) would proceed to the "off MAT with illicit use of opioids" state more frequently than subjects who successfully completed the run-in period and entered the full study. Of the 665 subjects in the US-13-0001 study who did not complete the run-in period, 23 (3.5%) failed for medical reasons (see Table 1, additional detail in the Appendix), which is consistent with the known safety profile of SL buprenorphine. Specifically, for the SUBLOCADE treatment arm, ICER should assume that 96.5% of the cohort starts in the "MAT with illicit use of opioids" state and 3.5% starts in the "off MAT with illicit use of opioids" state. Therefore, we recommend that ICER reassign the subjects who did not complete the run-in period for non-medical reasons to the same initial health state as those who completed the run-in period ("MAT with illicit use of opioids").	
3.	Recommendation 2: The model should assume the discontinuation rate for SUBLOCADE is at least as good as or better than the discontinuation rate for Generic SL bup/nal. The report assumes that the discontinuation rate for Generic SL bup/nal is less than an extended-release injectable buprenorphine. However, there is no reason to believe that Generic SL bup/nal would have a lower discontinuation rate than SUBLOCADE. Both treatments contain the same active partial mu-opioid receptor agonist, buprenorphine. Moreover, SUBLOCADE was designed specifically to overcome limitations of sublingual buprenorphine products, including daily medication adherence, consistent therapeutic level of buprenorphine over time and the need for supplemental buprenorphine. The lack of adherence to oral MAT is well-documented. In its model, ICER uses a network meta-analysis (NMA) based on trial US-13-0001, which compares SUBLOCADE to placebo, and a trial by Rosenthal, et al. (2013), which compares PROBUPHINE with open-label SL bup/nal and placebo. ICER's analysis estimates an odds ratio of discontinuation for Generic SL bup/nal relative to SUBLOCADE of 0.67 (95% CI of 0.28 to 1.61). Additionally, the confidence interval does not indicate a statistically significant difference in discontinuation rates for Generic SL bup/nal and SUBLOCADE. There are several trial design characteristics for the Rosenthal, et al. study that further limit our confidence in the estimated discontinuation rates for Generic SL bup/nal	We agree that there are differences in designs between the two studies included in the network meta-analysis that compares Sublocade to buprenorphine/naloxone. Adding these ten other trials into the network meta-analysis will not be helpful in quantitatively comparing Sublocade to buprenorphine/naloxone. After further review of the evidence base, we concluded that an indirect comparison of the two drugs is not feasible due to lack of data. Please see the above response on how this decision affects the model.

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	vs. SUBLOCADE including: an open label design, more frequent urine analyses (3 per week vs. 1 per week in US-13-0001), and the route of administration in the placebo arm (implant). This design likely would decrease retention in the placebo arm of the Rosenthal study, which, in turn, would have inflated the retention estimate for SL bup/nal compared to SUBLOCADE. Finally, ICER's NMA includes only Rosenthal et al. (2013), and does not consider evidence on SL bup/nal from 10 other available trials. We recommend ICER add these 10 trials to the network, as was done in the full NMA report Indivior submitted to ICER in June 2018, which would result in a HR for study discontinuation of 1.1 (95% CI: 0.73–1.58) for SUBLOCADE (300mg/300mg) relative to Generic SL buprenorphine.	
4.	Recommendation 3: The model should estimate abstinence rates for SUBLOCADE and Generic SL bup/nal using four studies identified by a comprehensive literature review. To compare the clinical effectiveness of SUBLOCADE vs. Generic SL bup/nal, the model assumes an abstinence rate of 41.3% for SUBLOCADE based on study US-13-0001 and an abstinence rate for Generic SL bup/nal equivalent to that observed for the control arm in the CAM2038 trial (27.4%). Given the known differences in study design—which the draft report acknowledges—a comparison based solely on these two studies offers more speculation than verification of abstinence. Instead of comparing abstinence based on the comparison of two clinical studies, we urge that ICER develop an NMA consistent with the approach ICER uses to compare discontinuation rates. Using four studies identified by a comprehensive systematic literature review of all published clinical trials of opioid agonist therapies (Ling et al., 2010; Rosenthal et al. 2013; RB-US-13-0001; and Lofwall et al. 2018), we recommend that ICER conduct an NMA of "overall percentage of abstinence by urinalysis" to derive probabilities of abstinence at week 24 of 46.4% and 22.8% for SUBLOCADE and Generic SL bup/nal, respectively (details of the calculation are provided in the Appendix). The literature review protocol, as well as detailed methodologies for this NMA, are presented in the full NMA report we submitted in June 2018. A sample Win BUGS code and data inputs from the four studies ready for Win BUGS entry are included in the Appendix to this letter.	Please see our second response in this section.

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5.	Recommendation 4: ICER should include additional evidence to capture the role of SUBLOCADE in supporting patients' recovery journey. • *Improved quality of life*: In the pivotal Phase III clinical trial, subjects receiving SUBLOCADE (both doses) versus placebo had significantly greater changes from baseline on the EQ-5D-5L visual analog scale (VAS) and SF-36 physical component score—demonstrating quality-of-life improvements. Differences in the EQ-5D-5L index with 300mg, VAS with 100mg, and SF-36 in both groups vs. placebo were found to be clinically meaningful based on published benchmarks established in other chronic conditions. Treatment satisfaction was reported by 88% of patients (both doses) of RBP-6000 and 46% of placebo-treated subjects (P<0.001 for both). • *Impact on improving return to work and/or overall productivity*: For those receiving SUBLOCADE in the RB-US-13-0001 study, employment increased by 10.4% on average while decreasing 12.6% for placebo patients.20 Those receiving SUBLOCADE worked approximately 4 hours more per week on average. Subsequently, in the long-term follow up of the participants of the SUBLOCADE Phase III programs, sustained levels of employment, low levels of health resource use and low prevalence of arrests throughout the 12 months of post-trial observation were observed among those who received SUBLOCADE. • *Longer SUBLOCADE treatment durations were associated with higher rates of opioid abstinence over 12 months*: Twelve months following enrollment in the RECOVER study, approximately half of those who participated in the SUBLOCADE Phase III program and recruited to the RECOVER study demonstrated complete, continuous abstinence, despite a low prevalence of any use of MAT. Further, longer SUBLOCADE treatment durations were associated with higher rates of opioid abstinence.	Thank you for sharing quality of life and productivity data for the comparison of Sublocade to placebo. However, our focus for the clinical evidence was the comparison to buprenorphine/naloxone. We would consider any clinical data available to that aim.
Clinicians		
James Andersen, MD, FASAM, ABAM		
1.	I would like to comment on some values of injectable buprenorphine beyond the exhaustive statistics in your report. With sex, age, and some details altered for privacy, I offer these cases for your consideration:	Thank you very much for sharing your experience with Sublocade and stories of patients who have used it.

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	A drug dealing, heroin addicted couple, incarcerated during the study, who were unable to keep their protocol defined visit windows. They both said "this was the best jail detox we've ever had. Didn't even feel it." Although neither designed nor powered to study this aspect of addiction, it was clear from this and other examples at the end of the trial that the drug eased out of the body so gradually that most subjects felt nothing. Four subjects which I followed post study in my office never even filled the end of study buprenorphine. They were not in withdrawal. A girl who had multiple psych issues, successfully completed the study and entered a drug free residential program elsewhere in the state. She did well, and one year later is not using. A gentleman who got a good job and promotions during the study, finished, didn't fill the buprenorphine rx and was fine until he took up with a former girlfriend who had continued to use heroin and suffered relapse. He is now back on buprenorphine films at 16mg per day. A 30 some year-old well- situated man who was drug free for over a year until he reacquainted with an old drug using "friend" who enabled him to use what he called "black tar heroin." After he overdosed, was resuscitated, hospitalized, and discharged he came to see me; his initial drug screen 2 days later was still positive for fentanyl. He was placed back on buprenorphine films but missed his next appointment. When he came in a week late he revealed that in wanting to use he would stop the films for a few days and then shoot up, then resume films when starting back in withdrawal. He and his non- using pregnant girlfriend agreed that he needed to be back on Sublocade which is now scheduled.	
2.	Quality adjusted life year statistics do not reveal the quality of the life that is saved by the use of a non-divertible, non-forgettable, continuous action effective product. Just from these few examples, it is evident that there are uses beyond the package insert for Sublocade which should be researched: preparation for entry into drug free programs when a person is spiritually, clinically, and psychologically ready, maintenance of sobriety for long term situations, ER treatment for stabilized OD's (most survivors leave asap	Rigorous outcome research studies are able to capture the different individual experiences you describe. More studies are needed, especially for a very new intervention such as Sublocade.

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	and return to their source of the very drugs which just almost killed them with 10% dead in a year), and better training for change to non-drug thinking (no having to take something every day to keep from "that feeling"-withdrawal).	
3.	If even half of the 60 000 or so persons who died of opioid overdose last year could have been successfully resuscitated and started on injectable long acting buprenorphine, the effect on families and friends and the nation would be incalculable. What can be calculated is the cost; I tend to look at the benefits in the cost/benefit ratio first. With 30 000 lives saved for another 30 earning years at just $30 000 earned per person per year, I see a $27 billion benefit. Adjusting for some subsidy, discount and insurance covering half the $1500 price of injection, adding this treatment to the current emergency mix would be adding only $22.5 million per year assuming no improvement in prevention strategies. Keeping all of those saved in a monthly (or longer) injection program would be expensive but not unrealistic at $270 million per year considering the latest federal opioid budget bill was $8.1 billion. I will leave it to ICER to work out the additional cost savings that could accrue from items such as reducing repeat OD'ers like one man who was recently reported to have been revived with ER Narcan 173 times in the last year at one Camden NJ ER which records 15 OD's per day.	Thank you for your comment. We have included societal costs where applicable and based on data availability.
Edwin A. Salsitz, MD, DFASAM		
1.	I was surprised that the issue of diversion of the sublingual and buccal formulations of buprenorphine was not mentioned, when discussing the subcutaneous formulations of buprenorphine. I would think that in addition to the usual outcome measures, the prevention of diversion is of paramount importance. Frequently patients are prescribed limited quantities of buprenorphine, necessitating frequent clinic visits, in an attempt to decrease the likelihood of diversion. The SC formulation would eliminate this concern, and in some cases allow patients more flexibility for work and educational activities.	Thank you for your comment. We have considered diversion in our assessment. However, it is important to note that a significant driver of diversion of buprenorphine transmucosal products is related to self-medication, especially in correctional settings. A significant proportion of diversion thus seems to be linked to difficulties in accessing MAT.
Payers		
Cigna		
1.	Our comments on the report focus on the availability of the medications reviewed (Sublocade, Probuphine, and Vivitrol) on payer formularies. An important distinction missing from the report's Summary of Coverage Policies	We have corrected this inaccuracy in the report.

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	and Clinical Guidelines is the difference between medications prescribed by a physician and dispensed by a pharmacy which fall under a patient's pharmacy benefit, and medications administered by a physician, which generally fall under a patient's medical benefit. The report indicates that Sublocade, Probuphine, and Vivitrol are not on Cigna's 2018 formularies, leading to an assumption that Cigna does not cover these medications. However, these medications are covered under Cigna's medical benefit, due to the manner in which they are administered (i.e., injected or implanted by a physician).	
Patient Advocacy Groups		
American Association for the Treatment of Opioid Dependence (AATOD)		
1.	We support the ICER approach and how it characterizes Medication Assisted Treatment for Opioid Use Disorder. It is important to recognize that Opioid Use Disorder is a chronic, treatable illness and long term treatment generally produces favorable outcomes, as repeatedly demonstrated by the National Institute on Drug Abuse and the Substance Abuse and Mental Health Services Administration. We also support the view as stated in the ICER report that "the primary aim of treatment is recovery rather than cure". This is still misunderstood by many addiction treatment providers and individuals who manage Drug Courts and correctional settings. We also support the view that the ICER report states that "all three drugs are to be used in combination with counseling and psychosocial support, described as a multipronged approach that includes counseling, vocational training, psychosocial therapies, family support, and building connections to community resources".	Thank you very much for your support for our work and your comments.
2.	We do not have comparable information on how support services are used when buprenorphine and other medications are used in a DATA 2000 practice or individual practices that decide to use long-term antagonists. All reasonable parties conclude, as ICER has, that such support services are needed to improve patient outcomes. Once again, it is important to go beyond the simple philosophic statements. We simply do not have the proper tracking mechanisms in place at the federal and state levels to determine how often such services are provided. This is a bottom line reality.	We agree that better knowledge of current service provision is needed.
3.	Finally, the report indicates that patients must attend daily to receive their dose of medication in OTPs. Patients typically get take-home medication, which	Thank you for your comment. We have adjusted the wording and removed the reference to daily visits.

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	progresses through the course of treatment. This is in accordance with the SAMHSA regulations, which specifies that OTPs must follow eight points of criteria when considering take-home medication. The point here is that it is not accurate to state that patients are always attending daily to get their treatment and medications in the OTP setting.	
4.	Our Association appreciates ICER's interest in this area. We have been observing with great interest the number of entities that have a new interest in evaluating the importance of treating Opioid Use Disorder and providing effective recommendations for the future. As individuals, who constructed this report will know, we have experienced several phases in this opioid use epidemic from prescription opioids to heroin and now more recently fentanyl. Services need to increase to respond to this demand but there needs to be much more focus on the quality of care that is delivered in addition to the harm reduction strategies that are being suggested. Medication alone is generally not adequate to respond to the many needs of patients who come into treatment. The focus has to be on ensuring that patients get access to good quality and coordinated care once medications are determined to be necessary in the treatment of this chronic disorder.	Thank you very much for your support for our work and your comments.
Addiction Policy Forum		
1.	Incorporate the societal costs of opioid misuse, addiction, and overdose into the cost/benefit analysis. As ICER develops a final report, ICER should more closely examine and incorporate the societal costs of opioid use disorder into its cost effectiveness analysis. These costs include not only lost productivity (for patients as well as their family members who spend time caring for them and mourning them when they die from substance-related causes) but also health care expenditures, criminal justice costs, child welfare, education, social services, and other costs. The burden of addiction and the opioid epidemic is borne by all of society, and these costs should be reflected in any analysis of the cost effectiveness of medications for treating opioid use disorder.	Thank you for your comment. Our model does include the costs of criminal justice and incarceration, in addition to the costs of lost productivity. However, due to data gaps, we could not include costs of child welfare, education, and social welfare. We hence label our societal perspective a "modified societal perspective."
2.	Consider the importance of providing medications that reduce the potential for diversion. ICER should consider the importance of providing medications that reduce the potential for diversion. This is important for at least two reasons. First, reduced diversion means that fewer	Thank you very much for your comment. We have considered diversion in our assessment. However, it is important to note that a significant driver of diversion of buprenorphine

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	opioids are available in our communities to people for whom they have not been prescribed who may be at risk for developing an addiction, in active addiction, or treating themselves for substance use disorder rather than seeking care from a health care provider. Second, reduced diversion will increase the comfort level among health care providers for treating patients with opioid use disorder with medications. We have a shortage of providers to treat patients on the scale required to arrest the opioid epidemic. In our conversations with providers, many are concerned about prescribing opioid medications for the treatment of opioid use disorder because they fear these medications may be misused or diverted away from their patients.	transmucosal products is related to self-medication, especially in correctional settings.
3.	Examine the adherence and quality of life benefits of long acting medications. ICER should consider the substantial benefits of long acting medications for opioid use disorder to improve medication adherence and the quality of life of patients and families. Medication adherence and a reduction in the ups and downs of blood concentrations of opioid medications are major benefits of these medications. People with addiction, especially those in the early stage of recovery, have to make the difficult decision every day to adhere to their treatment plan and medications while their addiction continues to hijack their brain and push them back toward active addiction. By making the decision to stay on medications a decision they have to make only monthly or even less often, we ease their road to recovery. Not only that, for those whose recovery is further along, they do not have to think every day about their need for medication. This can be a huge psychological benefit. Reducing the number of doctor's visits, trips to the pharmacy, or visits to Opioid Treatment Programs to receive medication means patients can focus more of their time and energy on addressing psychosocial needs and can reduce the burden on families to support the needs of their loved ones in treatment.	Thank you very much for your comments. These dimensions have been mentioned in the report, but they will be an important element in the discussions at the public meeting on November 8, 2018.
American Society of Addiction Medicine (ASAM)		
1.	ASAM is in support of the overall approach and conclusions of the draft evidence report. ASAM believes that the approach to culling research appears to be within usual and customary practices, and that the statistical analysis appears to be accurate – but recommends a biostatistician or epidemiologist to also review the statistical analysis. ASAM does recommend	Thank you very much for your comment. Our work has indeed benefited from external review processes by experts in different fields.

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	that the costs of medication should be an additional contextual consideration that will have an important role in the judgements of the value of the provided interventions.	
2.	ASAM believes the draft voting questions could potentially benefit from having some guidance as to how they are answered. It seems that asking whether LAI(X) is superior to transmucosal bup/nlx is simplistic, and one might struggle to answer without a definition of "superior." One suggestion is to pull this question apart into several questions with head-to-head comparison. In addition, ASAM recommends providing more options for questions 6-7. One suggestion for a question is: "What is the first line medication for the treatment of OUD?"	These are standard ICER questions for our panel. The panel understands the need to have discussions and context as they work through those. Thank you for raising these important issues, we understand the concerns, and we will use these notes as suggestions for things to cover during the policy roundtable session.
3.	Lastly, ASAM recommends separating questions 8-9 into each medication preparation. There may be specific considerations for each formulation, and ASAM believes that respondents should answer in the context of the specific formulation.	We revised our voting questions and we the NE CEPAC will be voting on Potential Other Benefits and Contextual Considerations for each drug separately.
Mental Health America (MHA)		
1.	In conducting the cost-effectiveness modeling, MHA asks that ICER consider cost-effectiveness from the perspective of both a generic payer and a public payer, i.e. Medicare and Medicaid. Medicaid and disability Medicare are the largest payers of behavioral health services in the United States. Poverty and disability contribute to the development of behavioral health conditions, and behavioral health conditions create burdens that can cause poverty and disability. Effective treatment and management of behavioral health conditions, on the other hand, can break this cycle and allow individuals to reach or maintain a level of community participation that positions them to stay on or purchase commercial insurance and not require public benefits – dramatically increasing cost-effectiveness from a public payer perspective. For ICER's cost-effectiveness modeling, this is different than the increases in productivity that ICER currently evaluates. With Medicaid and disability Medicare, increases in productivity beyond a threshold uniquely reduce health care costs as the individual disenrolls entirely or never requires coverage in the first place, impacting ICER's primary cost-effectiveness calculations for these public payers. Where there might not be adequate evidence to allow for modeling, even scenario analysis would benefit the field. By making such	Thank you for your comment. We have not included analyses specific to Medicare or Medicaid due to a lack of robust data on the effectiveness of MATs in these populations. We will consider your suggestions for future reviews, pending data availability.

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	analyses common practice, it can shift the paradigm for how CMS and state Medicaid agencies view costs and benefits, away from trimming health care costs and toward making critical investments that alleviate poverty and disability.	
Patients Rising Now		
1.	First, we recommend that ICER mirror the phrasing that it uses toward the end of the draft report: "OUD is considered a public health emergency with an epidemic of deaths that decrease the overall life expectancy in the US and impacts all parts of society: families, the health system, social services, the judiciary system, and the economy. For the affected person, OUD is a chronic disease that is often compared to other chronic diseases, such as diabetes, but that carries a stigma affecting self-esteem, social relations, and work." In contrast, the opening lines of the draft report characterizes the current crisis as an "increasingly common public health concern." We believe that this phrase – particularly at the start of the draft report – diminishes the significance and importance of the problem, and recommend that it be changed so as to not dilute anyone's impression about the seriousness of the problem. Overall, we recommend that ICER use the terms crisis, epidemic, or public health emergency.	We have adjusted the wording.
2.	Second, one of the many challenges facing the U.S. in responding to the opioid crisis is the historical stigma of the misuse or illegal use of opioids, and particularly heroin. As ICER notes, "This stigma is rooted in a widespread belief that drug addiction is a moral failing rather than a medical condition that is best addressed through treatment." And very recently, the Surgeon General released a report that noted the problems with access to MAT related to "the use of some medications for opioid use disorder (methadone and buprenorphine) remains surrounded by misconceptions and prejudices that have hindered their delivery." Some of that stigma is dissolving with greater understanding – and public appreciation – of the biological basis of OUD, but it is still a problem. Stigma not only inhibits individuals from seeking treatment, but can reduce the attention and resources that governments, payers, and clinicians will devote to the crisis. Therefore, word choices and language that reinforce that stigma should be avoided and those that help dispel it should be used. For example, people with opioid use disorder is preferred over addicts, and by extension avoiding the	We agree that it is important to avoid stigmatizing language and, as such, we did not use the term "addict" to refer to a person with OUD. However, the term "addiction" is still necessary and used by all stakeholders.

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	term addiction is preferred even though it has a place in technical clinical usage – and particularly to distinguish addition from dependence, a distinction that ICER's draft report touches upon.	
3.	Third, consistent with using language that does not reinforce the stigma of OUD, we recommend that ICER not use the term "Medications for Addiction Treatment" when referring to MAT. That term is used only rarely in the literature and is not used in SAMSHA's "Medications for Opioid Use Disorder" nor in other major documents and recommendations. In addition, we note in the draft report that MAT can be used by a person in recovery, i.e., in a state of dependence and not addiction: "A person in recovery refers to an individual who abstains from further use, reduces their substance use to a safer level, or takes steps to mitigate the potential physical and emotional harm resulting from continued use. A person can be considered in recovery while on MAT." Therefore, we urge ICER to use "Medication Assisted Treatment" as a definition for MAT because it is much more commonly used and a much less controversial – although we do recognize that this term also has problems related to whether the medication is the treatment or is assisting the treatment. That is, for other chronic diseases pharmacological therapies are also part of overall optimal treatment programs, e.g., diabetes, (where nutritional and exercise counseling are important), depression (where cognitive therapy can be important), and for other substance use disorders, such a nicotine dependence (where combining non-pharmaceutical therapies with a pharmacological agent can lead to better outcomes).	As indicated in background section, medication is the central element for effective addiction treatment. As required by the FDA and clinical practice guidelines, medication should be used in conjunction with psychosocial support. The World Health Organization uses the term "psychosocially assisted pharmacological treatment of opioid dependence." During the public consultation on the draft scope for our assessment, we received comments from clinicians to use the term "medication for addiction treatment," but to keep the acronym MAT, as all stakeholders refer to MAT as the combined use of medication and psychosocial support for treating OUD.
4.	And lastly, we recommend that ICER not refer to treatment or abstinence from opioid use as "cure" as it does in Table 4.3 and other places in the report. We realize that by putting the word in quotation marks ICER may be attempting to change the context of the word from a full cure to something else, but we believe that it would be better to avoid the word altogether. SAMHSA states that "OUD is often a chronic medical illness. Treatment isn't a cure." And as AHRQ wrote in a recent report, "Like other chronic diseases, opioid addiction cannot be cured but can be effectively treated and managed." Therefore, we assert that as with almost all chronic, biologically-based conditions, people are not cured of OUD any more than they would be cured of	Thank you for your comment. We have modified language in the report, and refrained from using "cure" where inappropriate.

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	diabetes or alcoholism even if they are able to manage their health without the use of medications, e.g., managing diabetes with diet and exercise is not a “cure” any more than having an acceptable hemoglobin A1C level with the use of medications is a “cure.”	
5.	The need for better access to treatments for OUD is a priority for many organizations, including the FDA, which is devoting resources to both developing better patient-focused outcomes for treating OUD, as well as expanding access to approved treatments, i.e., “Supporting development, access, and adoption of medications for treatment of OUD is a key priority of the U.S. Food and Drug Administration.” Therefore, we urge ICER in its documents and meetings to stress the importance of increasing access to all treatment options currently available for people with OUD, as well as exploring the importance of new treatments – particularly those that may use novel mechanisms of action. Like most complex chronic conditions, there are many avenues for treatment, and individualization of care is crucial for achieving the best outcomes.	As stated in the section on potential other benefits, ICER recognizes that "patients need to have access to different treatment options on their road to recovery" and that "extended-release formulations are important additional treatment options." These benefits will be presented together with the evidence on clinical and economic dimensions at the public deliberative meeting of the New England CEPAC on November 8, 2018. The resulting policy recommendations may include the dimension of improving access to MAT.
6.	As part of ensuring that access to all available treatments is recognized by ICER – and anyone who might come across ICER’s work – we believe that the current draft evidence report is deficient in its content by not fully recognizing methadone as a treatment option for OUD. Although, as ICER points out, access to Methadone is currently limited in the U.S., it is also clearly a part of the treatment guidelines referenced in Section 2.2 of the draft evidence report. By only partially summarizing (i.e., not including those guideline recommendations for methadone as part of MAT), the draft report fails to provide a complete picture of the recommended treatment landscape. And further, while current Federal and state laws and regulations restrict access to MAT with methadone, because those restrictions are not based in medical rationale, they could be changed to enable broader access – as is the case in other countries. And since ICER has stated that its goal is for a “more effective, efficient, and just health care system,” providing information and insights about options for care that could move U.S. health care delivery in that direction would be appropriate. In contrast, excluding methadone from the presentation in the draft evidence report undermines that effort since not only has methadone been shown to be clinically and cost effective,xx but with the tremendous need for	Thank you very much for your comment. Treatment outcomes with methadone are systematically described for every treatment outcome. However due to specific and stringent regulatory control as a Schedule II substance in CSA, transmucosal buprenorphine has been chosen as a comparator for the extended-release formulations, as outlined in the scope and the report.

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	individualized care, methadone should not be excluded from evaluations of treatment options by anyone – including payers, clinicians, or patients. We also note that both methadone and buprenorphine are in the WHO's Model List of Essential Medicines.	
7.	Another area of the draft report where methadone is not appropriately incorporated is its essential absence from the discussion of the various treatment options in ICER's quantitative analysis, i.e., it is not used alongside buprenorphine as a comparator even though the draft evidence report notes that it "dominated" buprenorphine in terms of cost and clinical effectiveness.	Due to specific and stringent regulatory control as a Schedule II substance in CSA, transmucosal buprenorphine has been chosen as a comparator for the extended-release formulations, as outlined in the scope and the report
8.	And on a technical note, we want to point out that ICER's description of the access limitations for methadone are somewhat imprecise. Specifically, the statement that that "access to methadone treatment is very limited in the US, as it cannot be legally dispensed through community pharmacies or physician offices, but only as part of highly structured treatment programs that patients must attend daily to receive their dose of medication," is technically incorrect because clinic visits of six days a week can be used at the start of treatment,xxiii and after a person has been engaged with methadone maintenance therapy for a while (i.e., they are stabilized and felt to be low-risk), weekly (or less frequent) visits may be required.	We have adjusted the wording and removed the reference to daily visits.
9.	Health care is still two words, not one.	Thank you for pointing out this oversight. We note that this does not affect the conclusions of our report.
10.	Footnote #67 has an typographical error – it is from 2015, not 2018.	We have corrected the date in the footnote.
Other		
California Health Benefits Review Program (CHBRP)		
1.	The California Health Benefit Review Program's (CHBRP's) faculty and staff that completed CHBRP's analysis on *Medication-Assisted Treatment* would like to suggest a clarification on how CHBRP's work was cited in ICER's draft report (on Page 10). The ICER draft report currently states: "A 2018 health technology assessment informing legislation in California that would require MAT for OUD concludes that "there is clear and convincing evidence that medications are more effective than a placebo or no treatment for retention of patients in treatment, abstinence from opioids, and a preponderance of evidence that receipt of medication reduces mortality."	Thank you very much for comment. The wording has been adjusted.

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	We would suggest a slight adjustment to more accurately characterize our work: "An analysis of legislation considered by the California State Legislature in 2018 concluded that "there is clear and convincing evidence that medications are more effective than a placebo or no treatment for retention of patients in treatment, abstinence from opioids, and a preponderance of evidence that receipt of medication reduces mortality." I believe this wording accurately describes our work without labeling it as a "health technology assessment" or any other term of art and without getting the reader bogged down with the particulars of the particular legislation considered by California. This modest clarification ensures that readers understand the specific statutory role that CHBRP plays in supporting California policymakers.	
MassBio		
1.	OUD is unlike other diseases, and the cost-effectiveness and value of specific treatment options needs to consider the differences between opioid agonist and antagonist medications. The draft ICER review fails to consider that each treatment is fundamentally different and that patients seeking each type of medication likely vary in their preferences, lifestyles, and where they are in their recovery journey. Each medication may offer unique value to the patient depending on these factors. To suggest that treatments are interchangeable based on cost can have negative consequences on limiting patients' access to these essential medicines.	The analytic framework used for our assessment provides a coherent approach for comparing the different extended-release formulations for the population of patients with OUD seeking MAT. As stated in the section on potential other benefits, ICER recognizes that "patients need to have access to different treatment options on their road to recovery" and that "extended-release formulations are important additional treatment options." These benefits will be presented together with the evidence on clinical and economic dimensions at the public deliberative meeting of the New England CEPAC on November 8, 2018. The resulting policy recommendations may include the dimension of improving access to MAT.
2.	ALL evidence-based treatments (including VIVITROL) have a role to play in turning the tide of OUD devastation, yet these treatments are significantly underutilized. Recent data reinforce that the conversation need not be about which medication is more effective but instead how we can improve access to and awareness of all FDA-approved treatments. Only broad awareness and access will allow people with opioid dependence to work with their physicians to find the right treatment plan to meet their evolving needs. As the only FDA-approved medication for the	Thank you very much for your comment. The importance of access to MAT and to individualized treatment will be discussed at the November 8, 2018 meeting.

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	prevention of relapse for opioid dependence following opioid detoxification, VIVITROL represents a distinct and important medication option for this critical and challenging public health issue. The cost of VIVITROL must be viewed in context and balanced against the cost of not offering treatment. Failure to offer such individualized treatment —treatment that the healthcare provider and patient feel is best suited to the needs and expectations of the particular patient at that particular point in time—can have negative consequences on both health outcomes and costs.	
3.	At MassBio, we believe that our work and advocacy must be patient-driven. This current opioid epidemic is a true public health crisis. Any analysis must take into account a real-world context. I am concerned that certain aspects of this report do not reflect the realities that patients suffering from OUD face each day as they work toward their recovery.	ICER strongly believes in integrating the patient perspective in our assessments, as outlined in our value assessment framework, which is available at https://icer-review.org/final-vaf-2017-2019/.