Report to the California Legislature

California's Cholinesterase Test Results Reporting and the Medical Supervision Program

Department of Pesticide Regulation
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

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EXECUTIVE SUMMARY

California's Medical Supervision Program ("Program") is designed to protect agricultural workers who regularly handle organophosphate and carbamate pesticides (OP/CB) (Title 3, California Code of Regulations, section 6728). The Program requires employers to contract with a medical supervisor to monitor the blood cholinesterase levels of these workers. The pesticides covered by the Program inhibit cholinesterase, an enzyme essential for proper neurological function. The California Department of Pesticide Regulation (DPR) is responsible for overall administration of the Program, with assistance from the Office of Environmental Health Hazard Assessment (OEHHA) in outreach and education of medical supervisors, and from the California Department of Public Health (CDPH) in approving laboratories performing cholinesterase testing.

The Program was established in 1974 when the use of cholinesterase-inhibiting pesticides was very prevalent in California agriculture. Pesticide Use Report data from 1995 to the present shows the use of all cholinesterase-inhibiting pesticides has declined nearly three-fourths. However, according to the most recent pesticide use data available, OP/CB use from 2008-2013 has remained between 4.1 to 5.1 million pounds per year. The Program has been reviewed on a number of occasions and updated to improve worker protection. It was most recently augmented in January 2011 when Health and Safety Code (HSC) section 105206 was implemented, requiring the reporting of laboratory cholinesterase test results to DPR. Under HSC §105206, DPR and OEHHA, in consultation with CDPH, are to collect and analyze cholinesterase test results and prepare a report for the Legislature by December 31, 2015. Unless extended by the legislature, the laboratory reporting and analysis will sunset on January 1, 2017. This report summarizes the review of the Program and test results, and presents findings and recommendations about the utility of laboratory reporting and the overall effectiveness of the Program.

From 2011-2013, DPR received over 90,000 cholinesterase test results from the reporting laboratories. A majority of the reported tests appeared to have been ordered for clinical reasons unrelated to the Program. Criteria were established to identify individuals undergoing cholinesterase tests who were likely in the Program. Spatial analysis of test results for this population further confirmed that these were likely workers in the Program as location of tests corresponded to regions of high OP/CB use. In addition to evaluating the pattern of cholinesterase test results, a medical supervisor survey (based on physicians ordering cholinesterase tests), inspection of growers in high-use OP/CB areas, and in-person visits with medical supervisors, augmented our knowledge of the overall effectiveness of the Program. The following provides findings and recommendations based on the analysis of the cholinesterase tests received and survey results.

Findings

DPR and OEHHA used multiple approaches to evaluate the effectiveness of the medical supervision program for illness surveillance and prevention and found that:

- Overall, the Program appears effective in protecting agricultural workers handling cholinesterase-inhibiting pesticides.
- Most individuals identified as part of the Program did not have depressed cholinesterase activity levels and when depressions occurred, most workers' activity levels recovered rapidly.
- Most medical supervisors who regularly ordered cholinesterase testing were aware of their responsibilities.
- Over half of the growers surveyed were familiar with the Program but had varying levels of understanding of specific requirements.
- Improvements in the electronic reporting system, further outreach to participants, and coordination across agencies responsible for the Program have significant potential to improve efficiency and performance.

On evaluation of the utility of laboratory-based reporting of cholinesterase testing for illness surveillance and prevention, DPR and OEHHA found that based on the data reported from 2011-2013, the utility of the data analysis is hampered by the inclusion of thousands of records from individuals who are not in the Program, and by missing data on the purpose of the test.

- Current laboratory-based reporting has some challenges such as laboratories reporting all cholinesterase tests regardless of their relevance to the Program; deficiencies in the electronic reporting system; and failure of some medical supervisors to communicate the purpose of the test to the laboratories.
- Certain assumptions were therefore made in order to evaluate the data. These assumptions introduced uncertainties in our findings and conclusions.
- DPR and OEHHA are working with the laboratories to improve their reporting, and conducting outreach to medical supervisors to emphasize the importance of including the purpose of the test on requisition forms. DPR and OEHHA plan to analyze the 2014-2016 data and provide an update to the Secretary of CalEPA by December 31, 2017, and thereafter, if reporting of cholinesterase test results is continued.

Recommendations and Future Directions

While the reporting requirements need to be improved to provide more targeted and accurate information, our review indicates the Program appears to be successful and current ongoing activities will help enhance its effectiveness including:

DPR/OEHHA - Recommendations	Lead Agencies/ *Participants*	Legislation Required
• Cholinesterase reporting should continue at least through December 31, 2018 in order to obtain additional data with clearer information on the purpose of the test and to allow further evaluation of the Program.	Leads: DPR, OEHHA *Participant: CDPH*	Yes
• Transferring cholinesterase reporting responsibilities from the laboratories to the medical supervisors may ultimately be a more efficient way to implement the Program.	Leads: DPR, OEHHA	Yes

DPR/OEHHA – Future Directions	Lead Agencies/ *Participants*	Legislation Required
• Enhance outreach and training to increase understanding of the Program by the medical supervisors, employers, laboratories, and the County Agricultural Commissioner (CAC) staff.		No
❖ Develop materials and conduct outreach efforts for the employers on their roles and responsibilities under the Program, such as, record retention of employees' cholinesterase test results and medical supervisor recommendations.	Lead: DPR *Participant: CAC*	
❖ Promote and expand the medical supervision training, emphasizing the provisions of HSC §105206 and continuing in-person visits to the medical supervisors.	Lead: OEHHA	
❖ Conduct focused headquarters inspections of Pest Control Operators similar to those that DPR conducted with growers.	Lead: DPR *Participant: CAC*	
❖ Increase the County Agricultural Commissioners' awareness of the Program; include a module on the Program during Enforcement Training.	Lead: DPR *Participant: CAC*	
❖ Coordinate with CDPH on outreach efforts to the laboratories. Develop clear requisition slips that require indication of the purpose of the cholinesterase test.	Lead: CDPH *Participant: DPR*	
• Continue coordination between DPR, OEHHA and CDPH to enhance the effectiveness of the Program.		No
❖ Improve reporting of information specified under HSC §105206(b).	Lead: DPR *Participants: CDPH, OEHHA*	
❖ Develop a list of currently active medical supervisors and update it regularly.	Lead: OEHHA	

I. INTRODUCTION AND BACKGROUND

A. Introduction

California's medical supervision program ("Program") monitors the activity of a key enzyme, cholinesterase (ChE) in the blood of agricultural workers who regularly handle Toxicity Categories I and II organophosphate (OP) and N-methyl carbamate (CB) pesticides (CCR Title 3, section 6728; see Appendix A1). ChE is critical for the normal function of the nervous system, and even transient reductions in ChE activity level can lead to toxic symptoms that are characteristic of these two pesticide classes.

This report was prepared in accordance with the provisions of California Health and Safety Code section 105206 (Appendix A2) to evaluate the effectiveness of the Program and the utility of laboratory-based reporting of ChE test results for pesticide-related illness surveillance and prevention. The report summarizes a larger body of work that was conducted to evaluate the Program. Details of these efforts can be found in the Appendices.

This report is a collaborative effort between the Department of Pesticide Regulation (DPR) and the Office of Environmental Health Hazard Assessment (OEHHA), in consultation with the California Department of Public Health (CDPH).

In addition to an evaluation of the reporting process and analysis of the ChE test results, we conducted supplementary activities to better evaluate the Program, such as: 1) surveying medical supervisors by mail, 2) conducting in-person visits with medical supervisors, and 3) inspecting employment records of a select group of employers in areas of high OP/CB use.

B. Background

California Medical Supervision Program

The Program was enacted in 1974 when OPs and CBs were some of the most commonly used pesticides in California agriculture. Their use has tapered off, however, according to the most recent pesticide use data available, OPs/CBs use from 2008-2013 has remained between 4.1 to 5.1 million pounds per year.

Both OPs and CBs work as a pesticide by inhibiting ChE, which breaks down the neurotransmitter acetylcholine, leading to the death of an insect. OPs and CBs can also affect humans by inhibiting ChE, and at high exposure levels cause a variety of acute symptoms of neurological poisoning. The acute symptoms, which include vomiting, diarrhea, and increased respiratory secretions, can sometimes mimic other illnesses, and sometimes people can be sub-clinically affected without showing major acute symptoms. Due to the potential for sub-clinical effects or misdiagnosis of the acute effects, it can be useful to test for the depression of ChE in order to identify potential overexposure.

Because it is difficult to directly measure the levels of ChE in the nervous system, red blood cell (RBC) ChE and plasma ChE are tested instead. RBC ChE is the same ChE found in the nervous system and is thought to better reflect the ChE enzyme in the nervous system.

Furthermore, different ChE-inhibiting pesticides have different binding affinities for either RBC or plasma ChE. For these reasons, it is useful to test for the depression of ChE in both RBC and plasma in order to identify potential overexposure. Additionally, individuals have varying ChE levels. Therefore, it is important for each individual to have a baseline value before they handle OP/CBs. An individual's ChE depression is more accurately detected when compared to their own baseline value. A more detailed discussion of OPs and CBs, their mode of action and human health effects can be found in Appendix A3.

The goal of the California Medical Supervision Program is to protect pesticide handlers from excessive exposure to OPs and CBs. It requires employers to contract with a licensed physician as a "medical supervisor" to periodically test the ChE level of workers who regularly handle these pesticides (Figure 1). For a more detailed description of the structure and requirements of the Program, refer to Appendix B1.

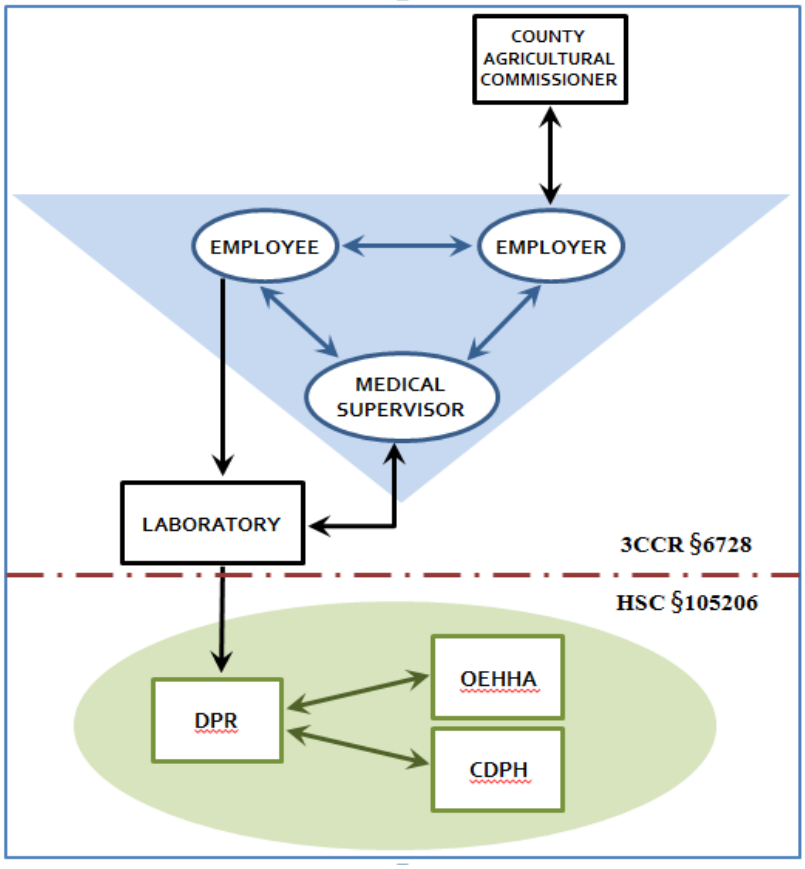


Figure 1: *Framework of the Medical Supervision Program.*

Since its inception, the Program has been reviewed on a number of occasions. These reviews have resulted in a number of recommendations that were adopted including: raising the "action threshold," changing the definition of workers that need to be under the Program, establishing the employee's individual ChE baseline value, using a specific analytical method to measure ChE levels, and specifying the frequency of testing. Additional changes, such as requiring employers to inform the medical supervisor of an employee's pesticide exposure status to determine the "purpose of test," and clearer guidelines for enforcement of the Program's requirements could improve the program. A more detailed description of the reviews, recommendations and implementation status can be found in Appendix A4.

Under the Program, employers who have an employee that meets the minimum regulatory requirement of regularly handling[1] OPs and CBs shall have a contract with a medical supervisor. The medical supervisor shall establish baseline values of RBC and plasma ChE during non-exposure periods for each employee, and periodically measure ChE activity levels while the worker handles OPs/CBs. If either RBC or plasma ChE is depressed below 80% of the baseline (that is, more than 20% depression from the baseline), it triggers an action response (Table 1). If a worker's ChE activity level drops more than 30% from the RBC baseline or more than 40% from the plasma baseline, he/she shall be removed from the exposure source. Following a worker's removal, his/her RBC and plasma ChE activity level must be monitored, and he/she is not allowed to work with or handle OPs and CBs until RBC and plasma ChE activity levels return to at least 80% of the baseline. The various RBC and plasma ChE depression levels discussed are called *action levels*, and they serve as a guide to protect workers from excessive exposure to OPs/CBs.

Table 1: *Action levels of RBC and plasma ChE and the associated actions required under the medical supervision program.*

% Depression from baseline	RBC ChE	Plasma ChE
≥20%	Prompt retesting of employee and evaluation of work practices by employer	
≥30%	Immediate removal of employee from further exposure	--
≥40%	--	Immediate removal of employee from further exposure

Health and Safety Code section 105206

In 2011, Health and Safety Code §105206 added a laboratory-based reporting requirement to evaluate the Program. Medical supervisors are now required to indicate the purpose of the test on the laboratory requisition slip. In addition, they shall ensure that the person tested receives a copy of the ChE test results, and any recommendations, within 14 days of receiving the results. Furthermore, the laboratories that perform ChE testing on human blood drawn in California as part of the Program are now required to report the test results, purpose of the test, specific information pertaining to the employee, his/her employer, the medical supervisor and the laboratory performing the analysis to DPR. ChE tests performed in response to a suspected or known exposure to ChE inhibitors that may or may not have resulted in illness are also included in the reporting requirement. Specific information on the required data elements that are to be included in a submitted report by the laboratories can be found in Appendix B2.

[1] "Regularly handle" is defined as mixing, loading, or applying pesticides for more than six days in a 30-day period (3CCR §6000).

Under HSC §105206 DPR shall share information from the ChE reports with OEHHA and CDPH on an ongoing basis. All information reported pursuant to this section shall be confidential, as provided in HSC §100330, except that OEHHA, DPR and CDPH may share the information with the appropriate county agricultural commissioner and local health officer for the purpose of surveillance, case management, investigation, environmental remediation, or abatement.

Upon completion of a report to the Legislature on December 31, 2015, laboratory reporting of ChE test results will continue until this reporting requirement sunsets on January 1, 2017. If the Legislature continues the reporting requirement beyond the sunset date, then laboratory analysis and data analysis will continue into 2017 and beyond.

II. FINDINGS

From 2011 to 2013, we received 91,093 ChE test results, representing 18,039 unique individuals, from the six laboratories approved by CDPH to perform ChE testing for occupational health surveillance. The data had to be manually reviewed to: identify and remove duplicates, correct formatting errors, identify missing information, and correct typographical errors. In addition to ChE tests ordered by medical supervisors under the Program, there are other reasons for ordering ChE tests such as pre-operative testing, Alzheimer's drug monitoring, liver disease screening, and aging research studies. Laboratories are not able to distinguish tests conducted under the Program from those that are performed for other reasons and therefore report all results to DPR. Extensive work had to be done to identify the results of tests that were conducted under the Program. We applied criteria to exclude individuals who were not likely part of the Program. For example, test results were excluded if the age of the

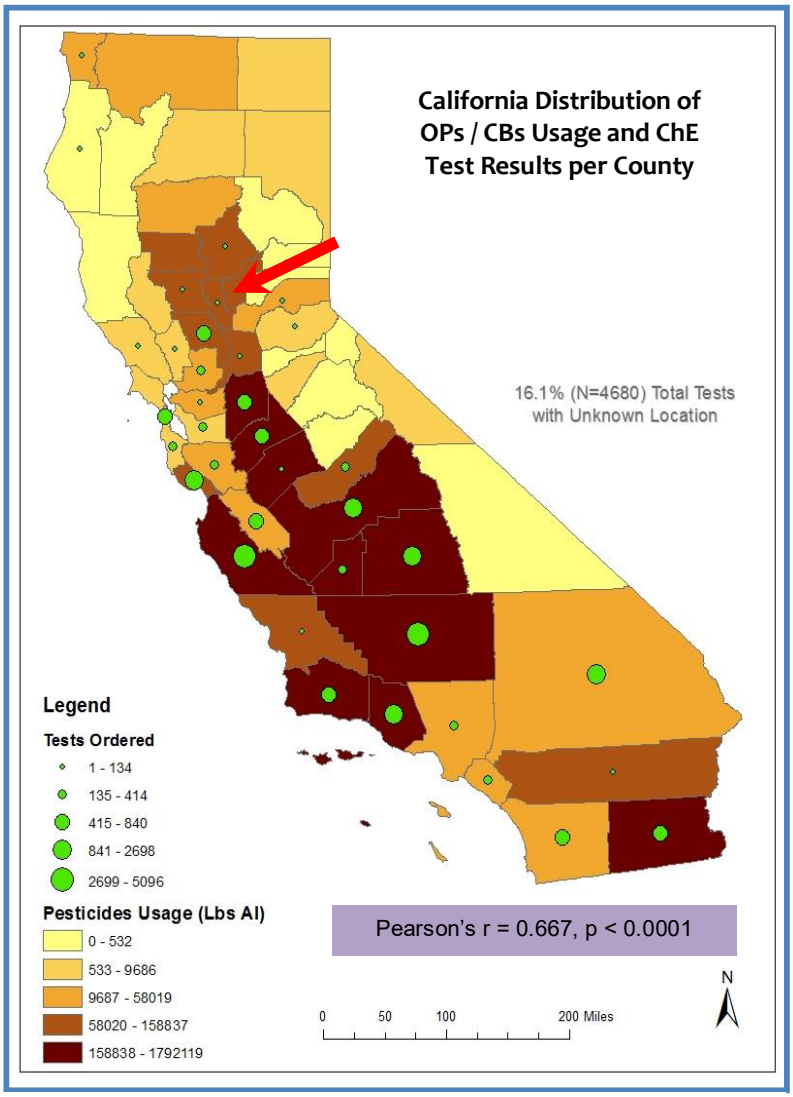


Figure 2: *Geographic distribution of OPs/CBs types I and II use (2011 – 2013) and number of ChE test results by county.*

patient was greater than 75 or less than 16; or if the test results were for RBC or plasma ChE but not both, as required under the Program. We analyzed the test results, relying on assumptions and inferences. In particular, the reports often contained incomplete or missing information related to the purpose of the test, making it necessary for us to make assumptions about which test results represented 'baseline' values, and which test results may have been post-application. Depending on how we assigned 'baseline' values, the frequency of potential ChE depression varied somewhat. To supplement the ChE test results analysis, we also conducted: 1) a medical supervisor survey by mail, 2) in-person visits with medical supervisors, and 3) on-site growers' headquarters inspections. See Appendices C, D, E and F for details on these activities.

Participation of Workers in the Program

After data review and exclusion of test results that were unlikely part of the Program, geographic analysis showed that there is a good correlation, as indicated by the Pearson's r value[2] (r = 0.667), between the number of test results by county and OP/CB use (Figure 2). The majority of the ChE test results were from the central region[3] of California which had the highest OP/CB usage. In addition, over half of the medical supervisors identified in the survey and from the in-person visits were from this area (Figures 3 and 4). Furthermore, the majority of the medical supervisors identified in the survey specialize in Occupational Medicine (Figure 4). Compared to other specialties, occupational medicine specialists are more likely to see patients for work-related agricultural cases, including workers who handle OPs/CBs.

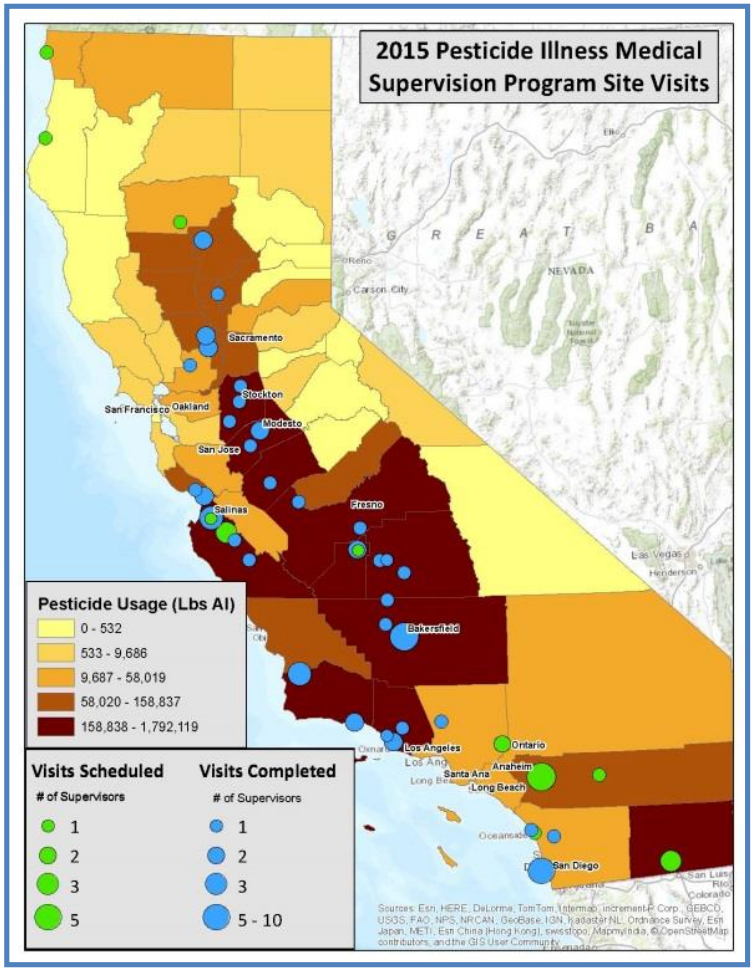


Figure 3: *Geographic distribution of OPs/CBs types I and II used (2011 – 2013), and location and number of in-person visits. (Total number of physicians visited, n=60)*

[2] Pearson's correlation coefficient (r) is a statistical measure of the strength of an association between two variables. The closer the r is to 1 or -1, the stronger the linear correlation. A value of 0 denotes no linear correlation.

[3] Based on DPR's Enforcement Branch's county distribution. Refer to Figure F1 in Appendix F.

However, geographic analysis also showed that there were very few ChE test results from some regions with relatively high OP/CB use (e.g., northern California counties represented by the red arrow in Figure 2). One possible explanation is that individuals in these high OP/CB use areas might not regularly handle these pesticides. This is supported by the focused headquarters inspection results which revealed that growers in this region did not have employees who regularly handled OPs/CBs (Figure 5). These growers stated that they limit their employees handling of OPs/CBs to six days or less in a 30-day period, although this could not be confirmed by pesticide use records. Additionally, three contracted medical supervisors interviewed in this region stated they had not seen patients who were under the Program so they had not submitted ChE test orders in the last few years.

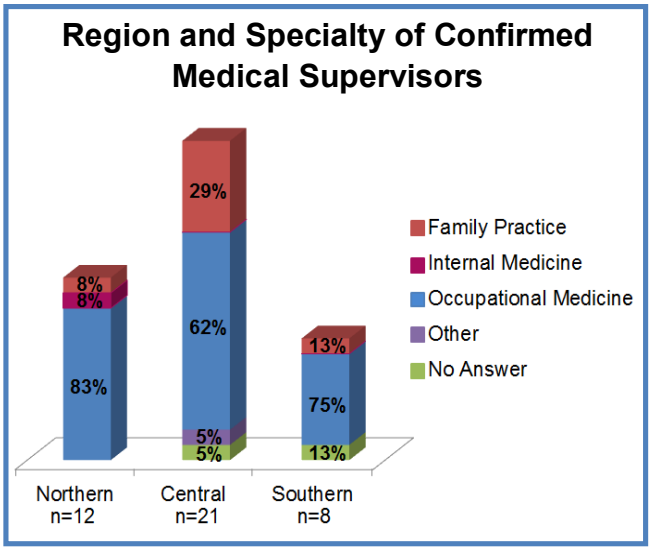


Figure 4: *Region and specialty of confirmed medical supervisors. (Total number of medical supervisors who responded to the survey, n=41.)*

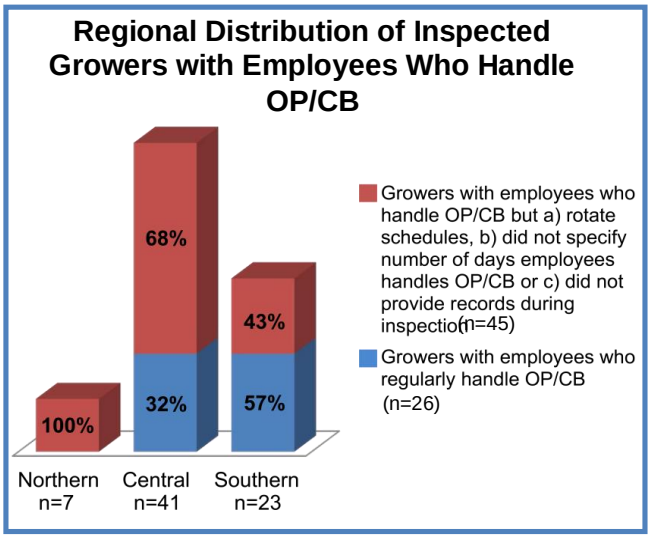


Figure 5: *Number of growers with employees who handle OP/CB by region. "Regularly handle" is defined as handling pesticides more than six days in any 30-day period.*

Patterns of ChE Activity Level and Frequency of ChE Depressions

There were 1,338 individuals who were tested numerous times over the three-year period, allowing a time course evaluation of ChE activity levels. Figure 6 represents five different patterns of individual ChE activity levels. These results illustrate variations in the frequency,

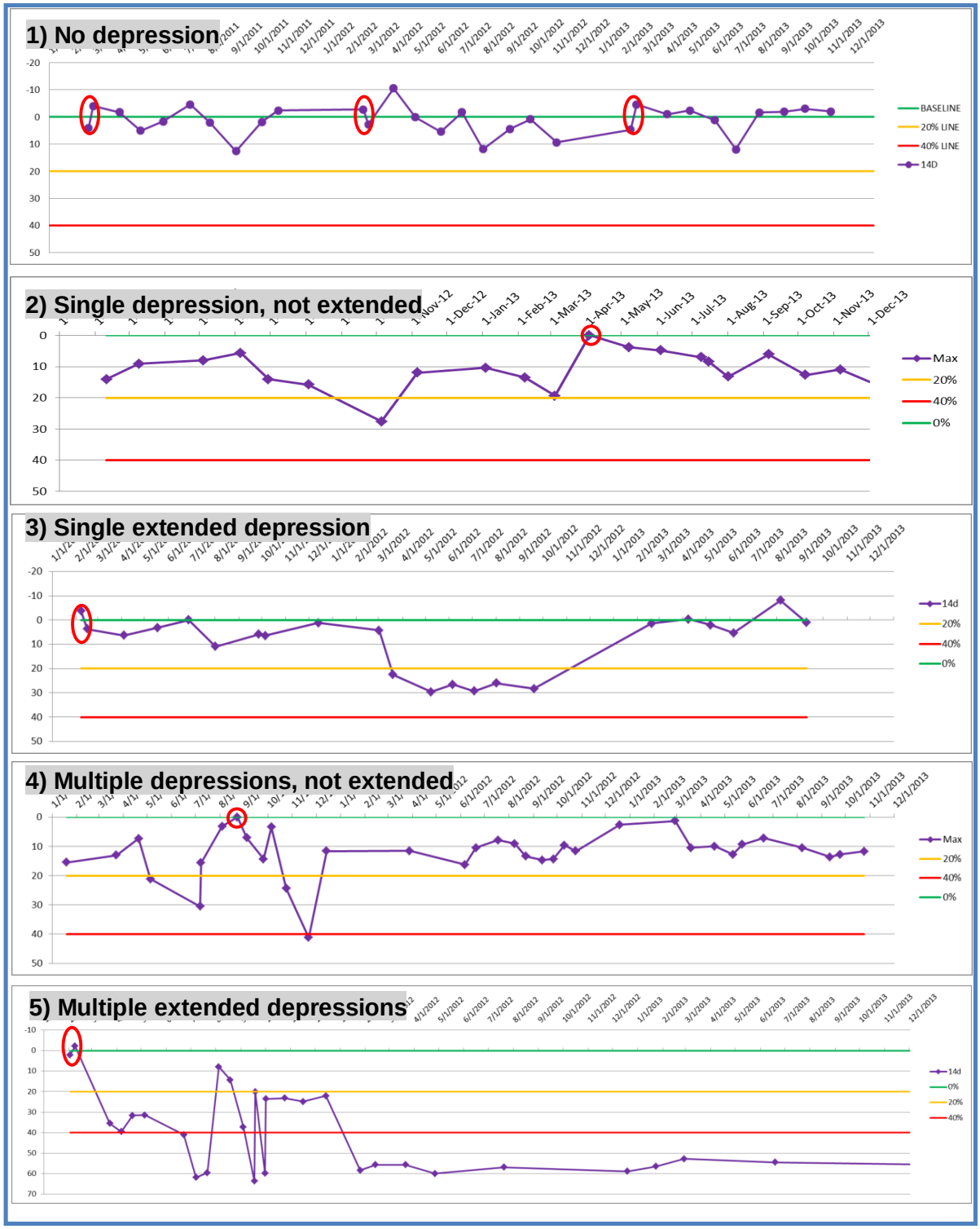


Figure 6: *Individual test results that represent different plasma ChE activity level patterns.* ***1)*** *no depression that exceeded action levels,* ***2****) single depression with prompt return to >80% of baseline level,* ***3)*** *single depression with slow return,* ***4)*** *multiple depressions with prompt return,* ***5)*** *multiple depressions with slow or no return. Y axis is percent depression from baseline. Green line represents the baseline of the individual. Red circled values are baselines.*

magnitude and duration of ChE depression that meet or exceed the various action levels (<80% of baseline estimate).

Of the 1,338 individuals who had multiple test results, about half (n=663) had a fairly clear 14-day baseline ChE value (that is, two blood samples collected 3-14 days apart during the non-spraying season) established according to the *Guidelines for Physicians*. These were identified as the most reliable baseline data ("Approach 1"). However, 14-day baseline estimates were not available for the rest of the population (n=675). In order to include these individuals in our analysis of depression frequencies, a more conservative approach ("Approach 2") was used. Approach 2 used each individual's highest ChE test result from 2011-2013 as an estimated baseline. Since a maximum ChE value could always be identified, Approach 2 was utilized in the analysis of all 1,338 individuals who had multiple test results. However, Approach 2 likely overestimates the percent of individuals with ChE depression.

We estimated the degree of over-estimation of baseline value introduced using Approach 2. The 14-day baseline estimate derived using Approach 1 was compared with the maximum value estimate derived using Approach 2 for those individuals who had both baseline values available. On average, the Approach 2 estimate of baseline was 12% higher than the estimate derived using Approach 1. Therefore, Approach 2 may overestimate the number of depressions that exceed one of the action levels.

It is worth noting that the need to use these two approaches to baseline determination arose because the test purpose was seldom provided with the ChE test reports. Consequently, baseline ChE values were inferred solely from the data.

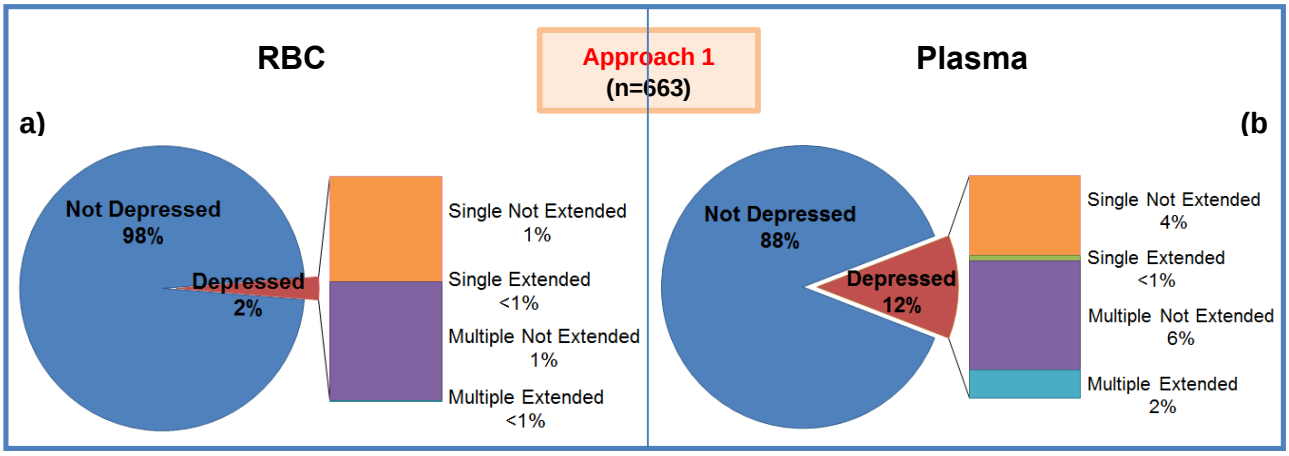


Figure 7: *Overall distribution of individuals (n=663) by type of ChE depression (single, multiple, extended or not extended) using* ***Approach 1*** *(14-day estimate of ChE baseline): RBC ChE (**a**) and plasma ChE (**b**).*

Of the 663 individuals that were analyzed using Approach 1, most had no ChE depression that exceeded an action level (98% based on analysis of RBC ChE results, 88% based on plasma ChE results) (Figure 7). This is consistent with findings from in-person visits with medical supervisors, who stated that they rarely saw cases with ChE depressions that required re-assessment of pesticide handling activities or removal of an employee from the workplace. Of the individuals with ChE depressions, we identified those who experienced depressions multiple times, and those whose depressions persisted for an extended period

of time[4]. Nearly all these depressions did not persist for an extended period of time ("not extended"), indicating prompt return to acceptable ChE activity levels (>80% of baseline value) and suggesting that action had been taken to reduce further exposure. However, some individuals experienced multiple ChE depressions (<2% based on RBC ChE results, 8% based on plasma ChE results). This suggests that, for these individuals, effective intervention to alter the work practices that led to exposure did not occur.

ChE activity levels in all 1,338 individuals were also evaluated using Approach 2 which, as discussed earlier, increases the likelihood that one or more of the action levels will be exceeded. As expected, the percentages of total ChE depressions, single and multiple depressions, and short-term and extended depressions were all higher when Approach 2 was used to identify baseline ChE value. For example, when Approach 2 was used, the percentage of individuals that had potentially experienced significant ChE depression increased to 13% based on analysis of RBC ChE results and 37% based on plasma ChE results.

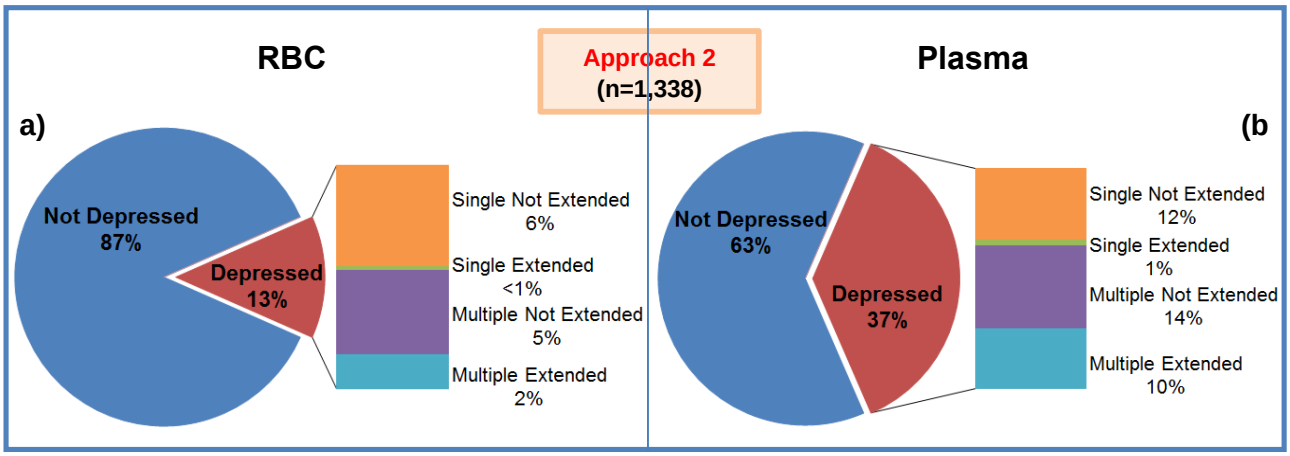


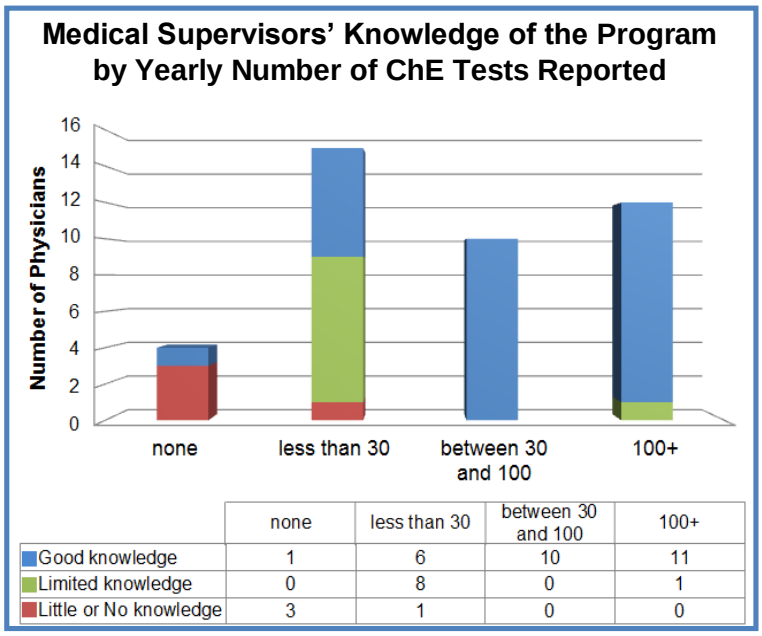
Figure 8: *Overall distribution of individuals (n=1,338) by type of ChE depression (single, multiple, extended or not extended) using* ***Approach 2*** *(maximum value estimate of ChE baseline): RBC ChE (**a**) and plasma ChE (**b**).*

We believe that the 14-day baseline is a better indicator of the "true" baseline because (1) it is consistent with the preferred method for baseline determination, as described in the *Guidelines for Physicians*, (2) two samples collected within a 14-day period provides additional support for the presumption that an individual participates in the Program, and (3) the second test result provides confirmation of the first baseline result. The maximum value baselines were on average 12% higher than the 14-day baselines. The use of the maximum value baseline, in effect, makes it more likely that an individual's test result will meet or exceed one or more action level. Therefore, even though Approach 2 includes data from all the individuals participating in the Program, the results obtained using Approach 1 (Figure 7) probably provides a more accurate reflection of the Program's effectiveness.

[4] At least three consecutive ChE test results that exceeded an action level within three months.

Level of Awareness of the Program by Medical Supervisors and Growers

The medical supervisor survey and in-person visits showed that most medical supervisors were aware of their responsibilities in the Program, and that there was communication between them and the growers. Feedback from the in-person visits indicated that medical supervisors who frequently ordered ChE tests were very knowledgeable about their responsibilities, and were more aware of Program changes and updates. Conversely, medical supervisors who ordered ChE tests less frequently tended to be less knowledgeable of the Program (Figure 9).



	none	less than 30	between 30 and 100	100+
Good knowledge	1	6	10	11
Limited knowledge	0	8	0	1
Little or No knowledge	3	1	0	0

Figure 9: *Level of medical supervisors' understanding of the Program based on the number of ChE tests they reported ordering within the last 3 years. (n=41)*

A medical supervisor was judged to have "good knowledge" or "limited knowledge" of the Program based on the interviewer's overall impression. In making this judgment, the interviewer considered the medical supervisor's (1) knowledge of Program's overall structure , (2) familiarity with the Guidelines for Physicians, (3) understanding of the medical supervisor's responsibilities, and (4) familiarity with Program updates (HSC §105206).

Although medical supervisors are not required to track the handling activities of individual workers, the medical supervisor survey indicated 44% were informed of the number of days an employee handled OPs/CBs while an equal proportion were not informed (Appendix D, Figure D4). This information was mostly provided by the employer and to some extent the employees themselves.

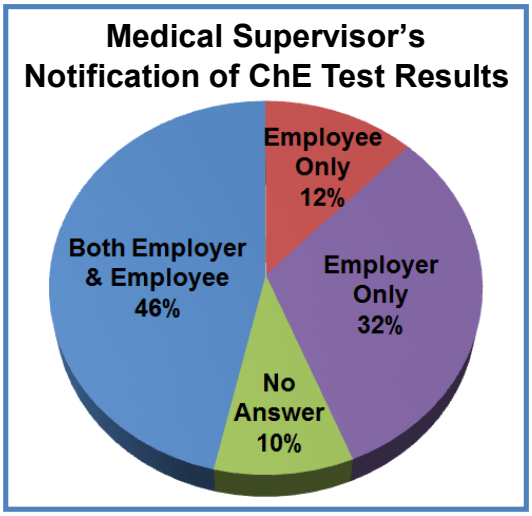
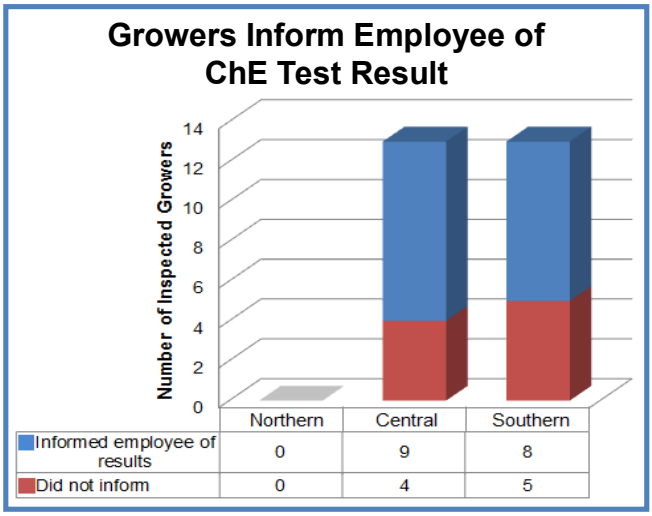


Figure 10: *Person notified by medical supervisor of the ChE test results. (Total number of medical supervisors who responded to the survey, n=41.)*



	Northern	Central	Southern
Informed employee of results	0	9	8
Did not inform	0	4	5

Figure 11: *Number of growers in the Program who informed employee of his/her ChE test results. (n=26)*

The medical supervisor survey indicated a majority of the medical supervisors notified the employee, the employer or both, of the employee's ChE test results (Figure 10). However, we do not know the extent to which the information provided was a copy of the actual laboratory report or a summary from the medical supervisor. We also do not know if the employee received this information within 14 days[5]. Some medical supervisors informed only the employer, and it is possible that these results were then relayed to the employee. This is supported by the information from the focused headquarters inspections that revealed two-thirds of the growers informed their employees of ChE test results (Figure 11). In instances where the ChE test results reached or exceeded action levels, over three-quarters of medical supervisors stated that they recommended an appropriate action for the employer to take (Figure 12). Although not a requirement of medical supervisors, it is good medical practice for physicians to follow up and confirm that employers modified their employees' work activities as recommended.

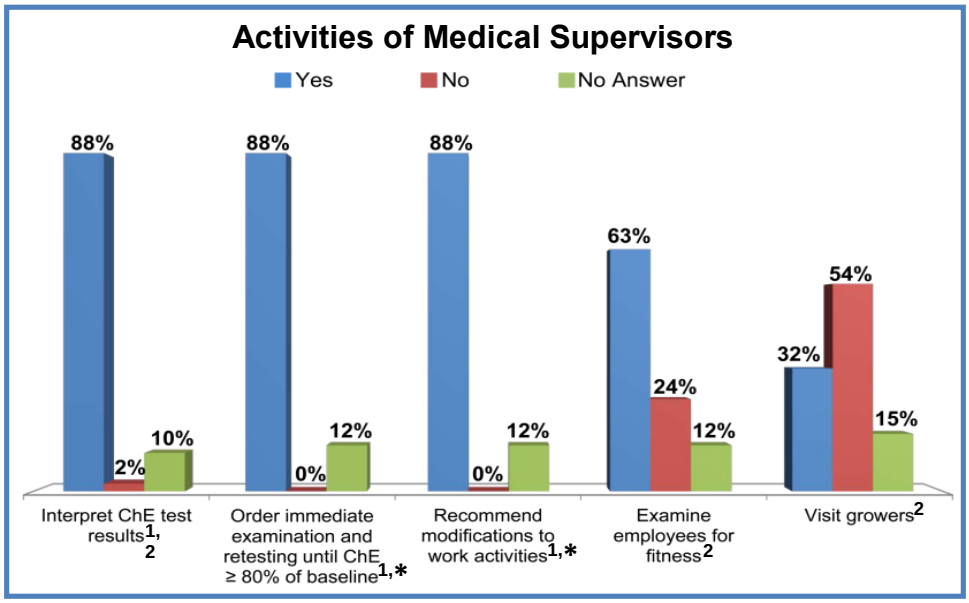


Figure 12: *Program required activities (1) of medical supervisors and those that are recommended in the Guidelines for Physicians (2). (Total number of medical supervisors who responded to the survey, n=41.)*
****** - When employee's ChE test results reach or exceed action level.*

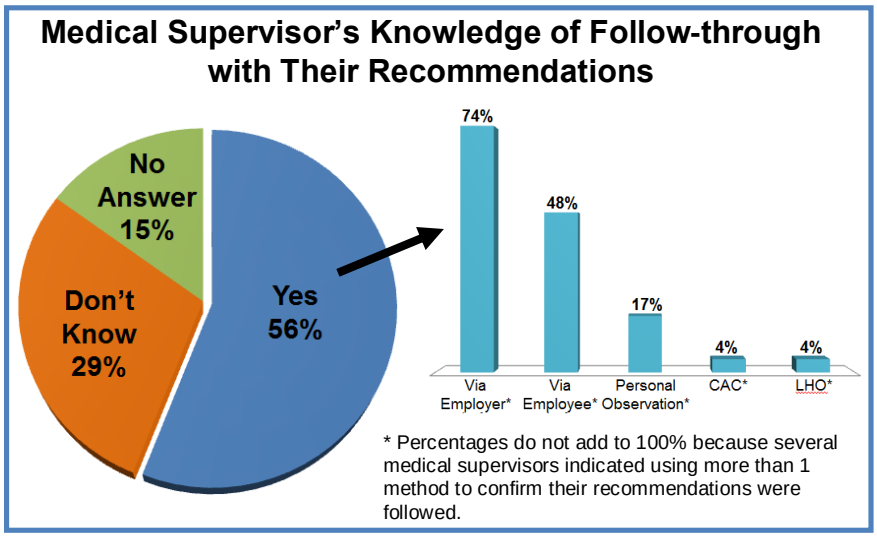


Figure 13: *Knowledge of follow-through with recommendations and method by which medical supervisors learned their recommendations were followed. (Total number of medical supervisors who responded to the survey, n=41.) CAC: County Agricultural Commissioner. LHO: Local Health Officer.*

[5] HSC §105206(c): medical supervisor ordering the test shall ensure that the person tested receives a copy of the ChE test results and any recommendations from the medical supervisor within 14 days of the medical supervisor receiving the result.

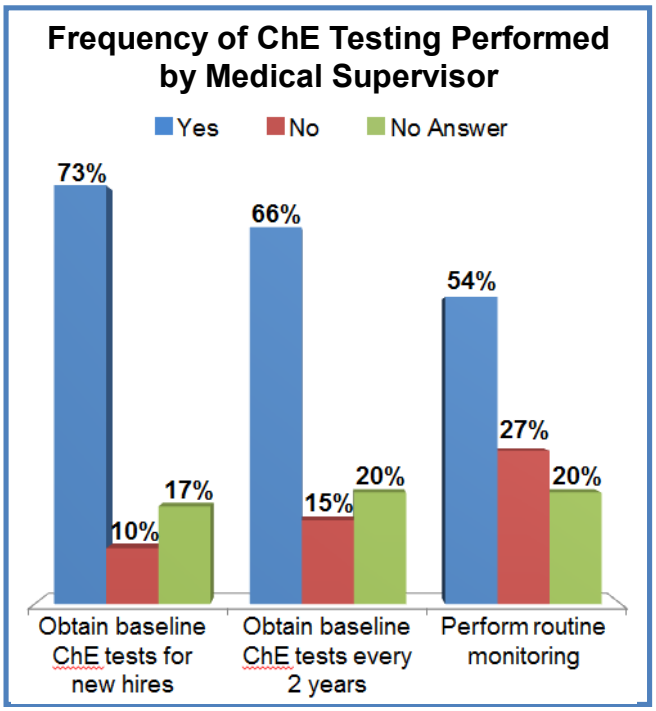


Figure 14: *Frequency in which medical supervisors obtain baseline for new hires, verify baselines and perform routine monitoring. (Total number of medical supervisors who responded to the survey, n=41.)*

with one of the primary findings of the focused headquarters inspections in which growers stated they managed their employees' schedules so that each employee would not have to handle OPs/CBs for more than six days in a 30-day period (Figure 5).

From the focused headquarters inspections, we found that over half of the growers were familiar with the Program but had varying levels of understanding of its specific requirements (Figure 15). A majority of the growers who are in the Program were aware of their responsibilities. Over half of these growers kept a copy of the medical supervisor agreement at their headquarters, with two-thirds of them providing a copy to the CAC. The same proportion of growers retained records[7] as required (Figure 16).

According to the medical supervisor survey, 56% knew that their recommendations were followed, mostly communicated through the employer (Figure 13). In addition, a third of the medical supervisors stated they have visited an employee's worksite as recommended in the *Guidelines for Physicians* (Figure 12).

Half of the medical supervisors surveyed stated they perform ChE testing for routine monitoring[6] (Figure 14). Less than a third did not and we do not know their reasons. Several medical supervisors interviewed in 2015 stated they no longer see patients who require ChE monitoring under the Program. This information is consistent

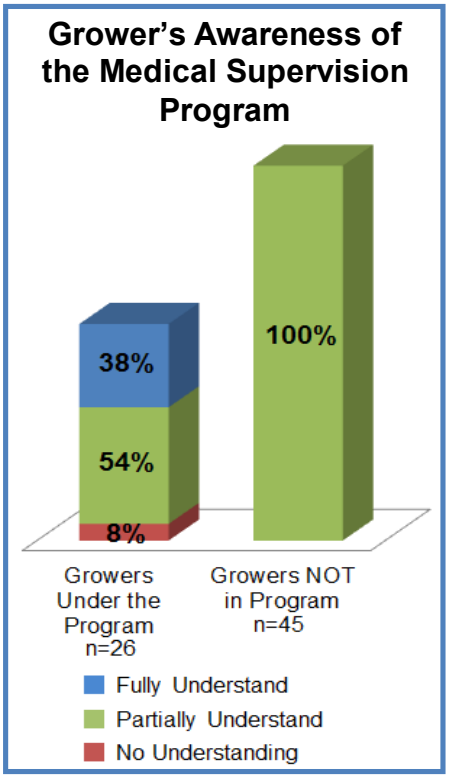


Figure 15: *Grower's level of understanding of the Program. (n=71)*

[6] 3CCR §6728(c)(2)(B) and (C): After three tests at 30-day intervals, further periodic monitoring shall be at intervals specified in writing by the medical supervisor. Where the medical supervisor has made no written recommendation for continued periodic monitoring, the testing shall be 60 days.
[7] 3CCR §6728(c)(3) states employer shall keep a record of the agreement with medical supervisor, OP/CB use records, all recommendations received from the medical supervisor, and all employee's ChE test results for 3 years.

Nearly all of the growers in the Program (n=25, 96%) received test results that did not reach action levels and, hence, did not require an investigation or modification of their employees' work practices. This is consistent with our analysis of the ChE test results which showed a low frequency of depression (Figures 7 and 8).

One grower indicated that he had an employee whose ChE activity level was below the laboratory's normal reference range. Having been informed of this by the medical supervisor, the employer voluntarily removed him from handling OPs/CBs (Appendix F, Figure F8). We do not know this employee's handling history or previous ChE test results. The grower took action based solely on this employee's single ChE test result.

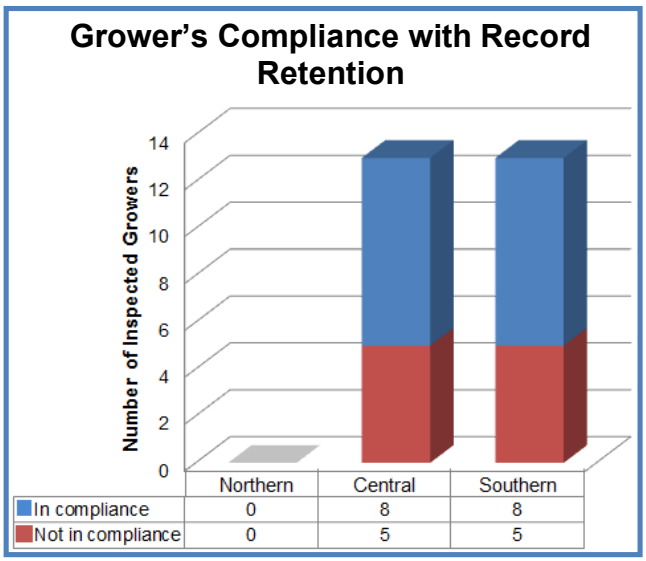


Figure 16: *Number of growers in the Program who retained their employee's ChE test results and medical supervisor recommendations. (n=26)*

Utility of Laboratory-Based Electronic Reporting

Reporting is an important tool for assessing exposure to OPs/CBs and prioritizing follow-up activities to improve worker safety. ChE test reports can be used to evaluate the Program and assess its effectiveness on a statewide basis. Combined with Pesticide Use Report data, these results allowed us to determine the correlation between the number of test results reported from a county and the amount of OP/CB used in that county (Figure 2). Areas where this correlation was not observed may warrant additional investigation. Furthermore, these reports allowed us to identify instances where a group of individuals showed a similar pattern of ChE depression (See Appendix C).

Our analysis of laboratory-based reporting (Appendix B) and ChE test results (Appendix C) helped us identify program elements that can be improved. For example, the distribution of individuals with ChE test results that exceeded action levels could be interpreted as an indicator of the effectiveness of the Program (Figures 7 and 8). Ideally, we would hope to see a minimal number of individuals with ChE depressions, or if they did have a ChE depression, it would not be repeated or prolonged, possibly indicating that the employer took action to prevent additional exposure. If an individual has repeated or prolonged depressions that exceed action levels, this suggests that long-term remedies are needed (e.g., implementing engineering controls, improving work practice, or providing better training to protect these workers).

For additional details on ChE data analysis, focused headquarters inspection, and medical supervisor survey and in-person visits, refer to the Appendices.

III. CHALLENGES

The current reporting structure presents some challenges in analyzing the data and evaluating the utility of this tool.

A. Submission of Cholinesterase Test Reports

Laboratories are aware of the required data elements to report and generate their own reports using our recommended Excel spreadsheet format. For the purpose of implementing a secure mechanism for electronic reporting, we utilized an existing web-based tool for laboratories to securely submit ChE reports to DPR. However, this tool merely transmits files so reports may still contain deficiencies (e.g., missing columns, duplicate records, typographical errors) that contributed to the difficulties we experienced in receiving complete data to analyze. Moreover, laboratories simply transmit the information but do not know whether individuals are workers in the Program, or the purpose of the test. See Appendix B2 for details.

B. Purpose of Cholinesterase Test

We currently receive all ChE test results from the six approved laboratories in California. Approximately three-quarters of the data appeared to be unrelated to the Program. Furthermore, the reports often contained incomplete or missing information related to the purpose of the test, the ordering physician and the employer.

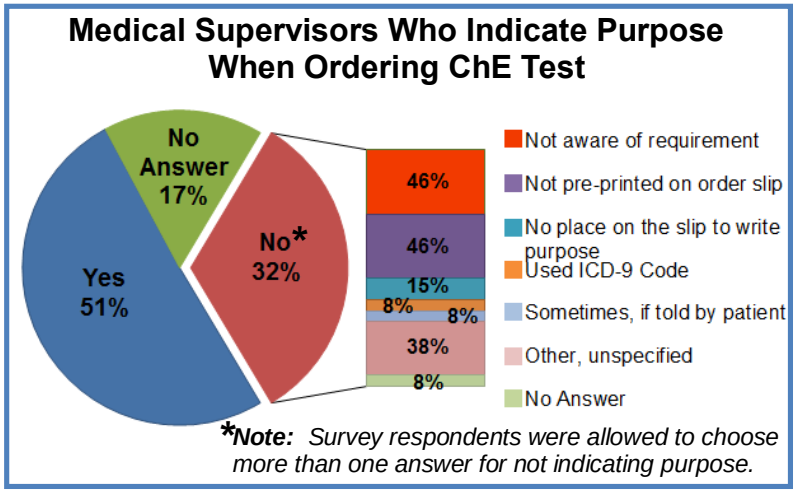


Figure 17: *Number of medical supervisors who indicated purpose of test when ordering ChE test and reasons for not indicating for those who do not indicate purpose of test. (Total number of medical supervisors who responded to the survey, n=41.)*

Although we sent letters to health care providers in 2011 reminding them of the requirement to indicate the purpose of ChE tests using specified terminology (see Appendix B2), only half of the medical supervisors in our survey reported that they indicate the purpose when submitting a ChE test requisition. Moreover, the ChE reports received continue to have a variety of 'purpose of test' entries, making it difficult to interpret in relation to the workers' pesticide handling activities. The medical supervisors who did not indicate the purpose of the ChE test stated that the main reasons were: 1) not being aware of the requirement, and/or 2) not having standard terms for purpose pre-printed on the laboratory requisition slip (Figure 17).

While most of the data elements required by HSC §105206 are straightforward, clearly conveying the purpose of the ChE test is complicated. It works on the premise that the employer, medical supervisor, their staff, and the drawing and/or reference laboratories all

have a common understanding of what is meant by the purpose of a ChE test as it relates to the patient's OP/CB handling activities. Unfortunately, this premise is not always reflected in the ChE test reports. This suggests that outreach to all involved parties, and a laboratory requisition slip containing all of the necessary information related to the Program, are essential to effectively utilize the electronic-based laboratory reporting tool. If the medical supervisors reported data directly to DPR, then all outreach and education efforts could be focused on this group of physicians.

Of the 91,093 test results received, 83.4% did not have a purpose entered. Of the 16.6% that had a purpose entered: 2.4% as 'baseline', 8% as 'periodic testing' (monitoring, follow-up, routine, etc.), 0.1% as 'exposure' and 6.1% as other entries (unavailable, CA test, etc.). See Appendix B2 for variations of entries for the purpose of test. The true purpose of these tests under the Program remains unclear because of: 1) the variety of entries for purpose reported (approximately 240 variations), and 2) the inaccuracy in the laboratories' interpretation of the purpose based on orders they receive. Without accurate information on the purpose of the ChE tests and ability to identify test results related to the Program, evaluating the data was challenging because we could not definitively identify the population of interest and we could not differentiate between baseline and routine periodic testing.

We used assumptions and inferences to develop exclusion criteria and used them to screen out ChE test results that may not be related to the Program. This not only increased the workload, but also could have led to misclassification of data.

To differentiate baseline test results from routine monitoring (follow-up) test results, we explored alternative methods to analyze the data (Figure 18). Analyzing three years of data (2011-2013) from the 1,338 individuals who appeared to be in the Program, about half (n=663) had two tests taken within 14 days during the low-spraying season[8]. Collection of two samples within a two-week time frame is consistent with the recommended procedure for baseline determination, as described in the *Guidelines for Physicians*. The baseline value for these individuals was calculated by averaging the results from these two tests, and this process was designated Approach 1. However, 14-day baseline estimates were not available for the rest of the population (n=675). In order to analyze the frequency of ChE depression of the entire population, the highest test result obtained over the 2011-2013 time period was used as an alternative estimate of the baseline value. This process was designated Approach 2, and we consider it to be more conservative because it likely leads to overestimation of the percent of individuals with ChE

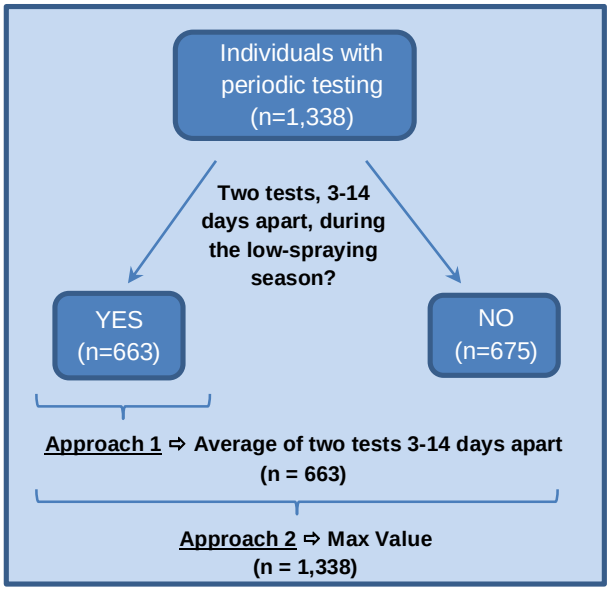


Figure 18: *Diagram of the two different approaches to determine baseline values for analysis.*

[8] Five months with the lowest OP/CB pesticide use in California: November through March.

depression. Nevertheless, Approach 2 allowed us to analyze data from all the individuals that had multiple test results because a maximum ChE value could always be identified.

Both of the approaches we used to determine the baseline ChE value are based on inferences and only provide estimated baselines. Results generated using these approaches are presented in the Findings section (Figures 7 and 8). These figures show large differences in the frequency of individuals with depressions using the two approaches (2 vs.13% for RBC ChE and 12 vs. 37% for plasma ChE). Regardless of the approach used, similar ratios were calculated for the four types of depressions (single vs. multiple and extended vs. not extended). Overall, both approaches showed that most individuals did not experience any type of depression.

C. Employee's Worksite

The employee's worksite could be used to assess the level of participation of workers under the Program. However, this information was not provided in the ChE test reports, nor is it required. To overcome this data gap, we used the physician's location as a surrogate for the employee's location to determine the correlation between test results and county-specific Pesticide Use Record data. This method may incorrectly assign an employee to a wrong county if that employee was seen by a medical supervisor located in a different county.

D. Employer Profile

Of the 71 focused headquarters inspections of growers who used OPs/CBs, only 26 indicated that they were in the Program (Figure 5). Although these inspections provided a snapshot of employers under the Program, it was a small sample and not representative of all of them. To obtain a more comprehensive understanding of the Program, we need to gather more information including inspections of Pest Control Operators who generally employ more workers that regularly handle OPs/CBs.

E. Accuracy of Medical Supervisor Information

We conducted ancillary activities to supplement our understanding of the Program such as: 1) a medical supervisor survey by mail, 2) in-person visits with medical supervisors, and 3) a focused growers' headquarters inspections to supplement our understanding of the Program. One of the major hurdles in conducting these activities was the absence of an accurate and complete list of medical supervisors and their contact information. We were unable to obtain this information from the ChE test reports due to the following:

- Information on the ordering physician is not always provided.
- The name provided in a laboratory report may not be a physician and/or medical supervisor. The person can be a non-physician who may or may not be working under the direction of a medical supervisor.
- The population of active medical supervisors appears to be dynamic. From 2011 to 2013, some physicians who had been identified as medical supervisors had retired or were no longer active, and others became medical supervisors after we had completed the data gathering process.

The lack of a complete and accurate list of medical supervisors prompted us to cast an extremely wide net when we conducted the medical supervisor survey. Indeed, of the physicians who were mailed a survey (n=699), we were only able to identify 6% (n=41) as being medical supervisors. An up-to-date list of medical supervisors would have facilitated and targeted our activities and is critical in conducting future outreach efforts. Our current outreach efforts led to identification of physicians who were previously not recognized as medical supervisors. We confirmed that they were medical supervisors through in-person visits.

IV. SUMMARY AND CONCLUSIONS

The Medical Supervision Program (3CCR §6728) was designed to protect the health and safety of pesticide workers who regularly handle cholinesterase-inhibiting pesticides, when OPs/CBs were the most commonly used pesticides to control insects. During the last 40 years, new insecticides have entered the marketplace and the use of OPs/CBs has declined.

HSC §105206 requires laboratories to submit to DPR ChE test results of workers handling OP/CB Toxicity Category I and II pesticides. The statute also requires laboratories to submit ChE test results for persons who were allegedly exposed or exposed to OPs/CBs and became ill from this exposure. DPR and OEHHA, in consultation with CDPH, are mandated to prepare a report on the effectiveness of the Program and the utility of the laboratory-based reporting of ChE for pesticide-related illness surveillance and prevention.

In this report, we evaluated the effectiveness and utility of the Program using data obtained from three different sources:

- information derived from the ChE test results
- feedback and suggestions provided by medical supervisors through a mail-in survey and in-person visits
- information obtained from growers' headquarters inspections

Utility of Laboratory-Based Reporting of ChE for Pesticide-Related Illness Surveillance and Prevention

We found the ChE data useful for evaluating specific requirements of the Program particularly when supplemented by physician surveys and visits, and grower inspections. However, its usefulness was limited because many of the reported test results were unrelated to workers in the Program, and by the lack of accurate information regarding the purpose of the ChE tests. When the ChE data is not accompanied by information on the purpose of the test and the worker's occupational history, the complexity and difficulty of analysis and interpretation are increased, therefore reducing the reliability of the findings.

We analyzed the geographic distribution of ChE tests and OP/CB use, and found a significant correlation, which indicates workers are participating in the Program where anticipated. We noticed there is a lack of correlation in some regions (e.g., Northern San Joaquin Valley). Information derived from inspections of growers' headquarters in those regions indicates most of their workers do not regularly handle OPs/CBs and, thus, are not

required to participate in the Program. Future in-person visits of medical supervisors and professional applicators in these regions may confirm this finding.

Effectiveness of the Program

While evaluating the Program, we identified possible improvements in communication that would help to more fully evaluate the Program and contribute to its continued success. For example, the manner in which information is conveyed among Program participants is not clear. Improvements in communicating ChE test results to employees and documenting whether a worker has been handling OPs/CBs for more than six days in a 30-day period would be useful. In addition, the Program requires the collaboration of various agencies (DPR, OEHHA, CDPH and the County Agricultural Commissioners), each with their own regulatory authority and responsibility. The Program also requires collaboration and communication between employers, workers, medical supervisors, and laboratories. Enhancing educational materials and outreach efforts to improve communication among all Program participants would strengthen our efforts to monitor the Program's effectiveness to enhance protection of California's agricultural workers.

Using information from the ChE data, feedback from medical supervisors, and reports from grower inspections, we conclude that overall, the Program appears to be effective in protecting agricultural workers handling OPs/CBs in California. Medical supervisors and growers are mostly knowledgeable about their respective responsibilities and roles in the Program. However, since the medical supervisors are responsible for several facets of the Program (e.g., evaluating the employee, submitting ChE test laboratory requisition forms, receiving ChE tests results from the laboratory, and informing the employee and the employer of the test results), it may make sense to also transfer the ChE reporting responsibility to the medical supervisors. This requirement could allow the agencies to target their education efforts to one group, and could facilitate more complete and timely reporting which will consequently enable prompt data analysis, evaluation and the determination of action levels when necessary.

While, due to the current reporting requirement and practices, it has been difficult to obtain accurate information, our analysis of the ChE data indicates a majority of individuals did not experience ChE depression. For those who did, most of them had their ChE level rebound within a short period of time, suggesting that the employer took corrective measures and prevented the worker from further exposure to OPs/CBs. However, we also found that some individuals had multiple short-term depressions in 2011-2013, suggesting that effective communication between medical supervisor and employer did not occur or exposure to OPs/CBs was not minimized and/or eliminated.

The survey and in-person visits revealed that most medical supervisors were aware of, and complied with, the requirements of the Program. However, not all medical supervisors were aware of the new provisions of HSC §105206. This suggests that further outreach to the medical supervisors is necessary to improve their understanding of the program and it's reporting requirements.

A major obstacle in conducting the survey and in-person visits was the absence of an existing registry of medical supervisors. As a result, we compiled our own list from submitted test reports that may not accurately capture the medical supervisors in the Program. The absence of an up-to-date registry of medical supervisors limits our ability to identify and survey medical supervisors, and also limits the effectiveness of our ongoing outreach efforts.

Information obtained from focused headquarters inspections indicated that while growers have a general understanding of the Program, they also have varying levels of awareness of some of the specific requirements. One finding is that some growers manage workers' schedules to limit their exposure to OPs/CBs to less than six days in a 30-day period. Of the growers participating in the Program, most did not have employees whose ChE test results required any action. However, the number of headquarters inspections conducted was small and focused on growers. Additional inspections of Pest Control Operators, who also employ pesticide handlers, would provide additional data on the Program. Despite the limitations of the reported ChE results, our analysis suggests that we identified workers in the Program and many of them did not have cholinesterase depressions in 2011-2013.

V. RECOMMENDATIONS AND FUTURE DIRECTIONS

Electronic-based reporting gives us the ability to analyze test results on a statewide scale. The survey and in-person visits with medical supervisors as well as the focused growers' headquarters inspections provided additional insight into the Program. The information from these various components helped identify program strengths as well as elements in need of further improvement. While most of our results supported the strengths of the Program, a proportion of workers still exhibited ChE depressions suggesting that workplace practices can be improved. The findings also indicate that growers and medical supervisors may not have a complete understanding of their responsibilities. All these results point to the following recommendations (Table 2) and future directions (Table 3):

***Table 2**: DPR and OEHHA Recommendations*

DPR/OEHHA - Recommendations	Lead Agencies/ *Participants*	Requires Legislation?
• The cholinesterase reporting should continue at least through December 31, 2018 in order to obtain additional data with clearer information on the purpose of the test and to allow further evaluation of the Program.	Leads: DPR, OEHHA *Participant: CDPH*	Yes
• Transferring cholinesterase reporting responsibilities from the laboratories to the medical supervisors may ultimately be a more efficient way to implement the Program.	Leads: DPR, OEHHA	Yes

***Table 3**: DPR and OEHHA Future Directions*

DPR/OEHHA – Future Directions	Lead Agencies/ *Participants*	Requires Legislation?
• Enhance outreach and training to increase understanding of the Program by the medical supervisors, employers, laboratories, and the County Agricultural Commissioner staff.		No
❖ Develop materials and conduct outreach efforts for the employers on their roles and responsibilities under the Program, such as, record retention of employees' cholinesterase test results and medical supervisor recommendations.	Lead: DPR *Participant: County Agricultural Commissioner*	
❖ Promote and expand the medical supervision training, emphasizing the provisions of HSC §105206 and continuing in-person visits to the medical supervisors.	Lead: OEHHA	
❖ Conduct focused headquarters inspections of Pest Control Operators similar to those that DPR conducted with growers.	Lead: DPR *Participant: County Agricultural Commissioner*	
❖ Increase the County Agricultural Commissioners' awareness of the Program; include a module on the Program during Enforcement Training.	Lead: DPR *Participant: County Agricultural Commissioner*	
❖ Coordinate with CDPH on outreach efforts to the laboratories. Develop clear requisition slips that require indication of the purpose of the cholinesterase test.	Lead: CDPH *Participant: DPR*	
• Continue coordination between DPR, OEHHA and CDPH to enhance the effectiveness of the Program.		No
❖ Improve reporting of information specified under HSC §105206(b).	Lead: DPR *Participant: CDPH, OEHHA*	
❖ Develop a list of currently active medical supervisors and update it regularly.	Lead: OEHHA	

VI. ON-GOING ACTIVITIES

To address some of the issues identified, we initiated the following activities:

A. The Online Monitoring Tool

DPR is working with the University of California, Davis on an online tool to capture data required by HSC §105206. This tool can improve communication between medical supervisors and reference laboratories. It can also enhance the data quality and the timeliness of ChE test results submission by the laboratories, and provide the data needed to adequately assess the utility of the program to reduce or eliminate agricultural worker health effects from handling OP/CB pesticides. Meanwhile, DPR will continue to work with the laboratories to improve reporting of the information required by HSC §105206. Details on this tool can be found at: http://pesticide-education.phs.ucdavis.edu/CholinesteraseMonitoringTools.php.

B. OEHHA's in-person visits to medical supervisors

OEHHA has conducted in-person visits and trainings with 70% of the 87 medical supervisors it has identified, and is conducting telephone interviews and trainings with the remainder. OEHHA intends to continue periodic in-person meetings with medical supervisors. The purpose of these visits is to: 1) inform them of the reporting requirements under HSC §105206, 2) provide a copy of the 2015 *Guidelines for Physicians* and a list of available training resources, 3) remind them of their responsibilities as medical supervisors; 4) obtain feedback on how medical supervisors implement the Program. Assessing the impact of this outreach on the quality of electronic laboratory reporting and the implementation of the Program will be useful in targeting future efforts and identifying resource needs. See Appendix E for additional information.

C. DPR working with CDPH on laboratory approval process

Following a meeting in June 2015, DPR initiated discussions with CDPH on the process for certifying laboratories that perform ChE tests. The purpose of these discussions is to find ways that may allow CDPH to ensure adequate quality control of the analytical methods for the cholinesterase test and for DPR to collect better information from the laboratories.

VII. GLOSSARY OF TERMS

3CCR §**6728**: Title 3, section 6728 of the California Code of Regulations, on Medical Supervision

AB 1963: Assembly Bill that added the Health and Safety Code section 105206 requiring California Department of Public Health-approved laboratories to submit cholinesterase test results of workers under the medical supervision program to the Department of Pesticide Regulation. AB 1963 was signed by the governor in September 2010 and became law on January 1, 2011.

Accession Number: A unique number assigned to each blood specimen by the laboratory submitted for analysis. The accession number protects a patient's privacy by functioning as a unique identifier rather than using the patient's name or other personal identifier.

Action Levels: A depression in the level of cholinesterase activity that meets one of the following thresholds:

- If either red blood cell or plasma cholinesterase is depressed below 80% of the baseline (that is, more than 20% depression from the baseline), it triggers a reassessment of work activities.
- If a worker's cholinesterase level drops more than 30% from the red blood cell baseline or more than 40% from the plasma baseline, he/she is removed from the exposure source.
- Following a worker's removal, his/her red blood cell and plasma cholinesterase must be monitored, and he/she is not allowed to work with or handle Toxicity Categories I and II organophosphate and carbamate pesticides until red blood cell and plasma cholinesterase levels return to at least 80% of the baseline.

Baseline: Red blood cell and plasma cholinesterase determinations measured prior to an employee's exposure to Toxicity Categories I and II organophosphate and carbamate pesticides. By regulation, a baseline cholinesterase test is required of all employees who will "regularly handle" these pesticides regardless of the frequency of subsequent monitoring. Once the baseline is determined, subsequent test results are evaluated as a percentage of the baseline activity.

Carbamate (CB): An organic compound with structural features that result in inhibition of cholinesterase enzymes, which are critical to normal function of the nervous system. Aldicarb, carbofuran, carbaryl (Sevin®) and methomyl are examples of carbamate pesticides.

CDPH: California Department of Public Health

Cholinesterase (ChE): An enzyme that catalyzes the hydrolysis of the neurotransmitter acetylcholine, and helps the nervous system to work properly. Under the Medical Supervision Program, two types of cholinesterase (plasma and red blood cell (RBC)) are required to be measured for all covered employees to account for the differences in the mode of action of cholinesterase-inhibiting pesticides.

- **Plasma Cholinesterase**: Considered to be more labile than red blood cell cholinesterase and is thus less reliable in reflecting actual enzyme depression at neuro-effector sites. It is generally more rapidly inactivated by exposure to organophosphates/carbamates.
- **RBC Cholinesterase:** Biochemically the same enzyme as the acetylcholinesterase located at the neuro-effector cell synapses. It is often depressed more slowly than plasma cholinesterase by exposure to organophosphates/carbamates.

County Agricultural Commissioner (CAC): Primary enforcement agents, at county level, for the State pesticide laws and regulations, and local ordinances.

DPR: Department of Pesticide Regulation, a department of the California Environmental Protection Agency.

Drawing Laboratory: Any laboratory that collects specimens (i.e., draws blood) from tested persons. Although these laboratories perform basic analyses, they send complex or infrequently ordered laboratory tests to a reference laboratory for analyses.

Guidelines for Physicians: The document, *Guidelines for Physicians Who Supervise Workers Exposed to Cholinesterase-Inhibiting Pesticides*, prepared by the Office of Environmental Health Hazard Assessment. This handbook describes the medical supervision program and the responsibilities of the medical supervisors. The 5th edition of this document was released in 2015.

Handler: Any person who:

i. Mixes, loads, transfers, or applies pesticides.
ii. Cleans, adjusts, handles, or repairs the parts of mixing, loading, or application equipment that may contain pesticide residue.
iii. Acts as a flagger.

HSC §**105206**: Health and Safety Code section 105206, codified into law by the enactment of AB 1963, that took effect on January 1, 2011. This section shall remain in effect only until January 1, 2017, and as of that date is repealed, unless a later statute enacted before January 1, 2017, deletes or extends that date.

Laboratory Requisition Slip: Form provided by the laboratories for ordering physicians to use when submitting specimen samples for analysis.

Medical Supervisor: Under HSC §105206, a licensed physician (M.D. or D.O.) who has a written agreement with employers of agricultural workers who regularly apply cholinesterase-inhibiting pesticides in Toxicity Categories I and II, to examine the employees for fitness, order cholinesterase tests, and to make the necessary recommendations based on the results of an employee's cholinesterase test results.

OEHHA: Office of Environmental Health Hazard Assessment, a department of the California Environmental Protection Agency.

Organophosphate (OP): A general term for esters of phosphoric acid that constitute the common structural element of many insecticides. These pesticides are toxic because they inhibit cholinesterase enzymes and impair normal function of the nervous system. Organophosphates are a large class of commercial pesticide products; examples include parathion, malathion, chlorpyrifos, and naled.

Pesticide Use Report (PUR): A comprehensive report of all agricultural pesticide use in California. Use data are submitted monthly to County Agricultural Commissioners, who in turn, report this data to the Department of Pesticide Regulation.

"Program:" Medical Supervision Program (3CCR §6728) as used in this document.

Purpose of Test: Under HSC §105206, a medical supervisor must indicate on the test order the reason for ordering cholinesterase tests for an employee.

- **Baseline**: Pre-exposure test ordered to establish the individual's normal level of a worker under medical supervision.
- **Routine (Monitoring)**: Test ordered for *periodic testing/follow-up assays* of a worker under medical supervision.
- **Event (Evaluation of suspected pesticide illness)**: Test ordered to identify effects of a suspected or reported pesticide exposure.

Reference Laboratory: An independent referral or diagnostic facility equipped with state-of-the-art equipment, and trained personnel to conduct various types of tests not otherwise available in most laboratories. Hospitals, laboratories and physicians will often use a reference laboratory for more complex or less frequently utilized tests.

Signal Word: One word used to indicate the acute toxicity of the formulated pesticide product.

i. **Danger**: Highly toxic by at least one route of exposure.
ii. **Warning**: Moderately toxic if ingested, absorbed through the skin, or inhaled.
iii. **Caution**: Slightly toxic if eaten, absorbed through the skin, or inhaled.

Toxicity Categories I and II: Refers to U.S. Environmental Protection Agency's classification system for pesticides that addresses the acute toxicity of these products.

i. **Toxicity Category I**: Highly toxic; Signal word "Danger."
ii. **Toxicity Category II**: Moderately toxic; Signal word "Warning."

Appendix A: BACKGROUND

1. California Code of Regulations, Title 3, section 6728. Medical Supervision

(a) Whenever an employee mixes, loads, or applies a pesticide with the signal word "DANGER" or "WARNING" that contains an organophosphate or carbamate, for the commercial or research production of an agricultural plant commodity, the employer shall maintain use records that identify the employee, the name of the pesticide, and the date of use. The original or copies of documents otherwise required to be maintained by this chapter may be used to meet the requirements of this Section provided they contain the information required by this Section.

(b) Each employer who has an employee who regularly handles pesticides specified in (a) shall have a written agreement signed by a physician, that includes the names and addresses of both the physician providing the medical supervision and the employer responsible for the employees, stating that the physician has agreed to provide medical supervision and that the physician possesses a copy of, and is aware of the contents of the document "*Medical Supervision of Pesticide Workers-Guidelines for Physicians*" (available from the Office of Environmental Health Hazard Assessment). A copy of this agreement shall be given to the commissioner by the employer no later than when an employee begins to regularly handle pesticides specified in (a).

(c) The employer's responsibilities for medical supervision for employees regularly handling pesticides specified in (a) shall include the following:

(1) All covered employees shall have baseline red cell and plasma cholinesterase determinations. Baseline values shall be verified every two years. For new employees, the medical supervisor may accept previously established baseline values if they are obtained in accordance with these regulations by the same laboratory methodology and are acceptable to the laboratory which will analyze the new employee's blood samples.

(2)(A) The employer shall ensure that each employee, not previously under medical supervision associated with that employer, has red cell and plasma cholinesterase determinations within three working days after the conclusion of each 30-day period in which pesticides specified in (a) are regularly handled.

(B) After three tests at 30-day intervals, further periodic monitoring shall be at intervals specified in writing by the medical supervisor except for verification of baseline as specified in (1).

(C) Where the medical supervisor has made no written recommendation for continued periodic monitoring, the testing interval shall be 60 days.

(3) The employer shall keep a record of the agreement to provide medical supervision, use records, all recommendations received from the medical supervisor, and all results of cholinesterase tests required to be made on his/her employees by this Section or by the medical supervisor. Records required by this Section shall be maintained for three years and shall be available for inspection by the employee, the Director, commissioner, county health official, or state health official.

(4) The employer shall follow the recommendations of the medical supervisor concerning matters of occupational health.

(5) The employer shall post the name, address, and telephone number of the medical supervisor in a prominent place at the locale where the employee usually starts the workday; or if there is no locale where the employee usually starts the workday, at each worksite; or in each work vehicle.

(d) The employer shall investigate the work practices of any employee whose red cell or plasma cholinesterase levels fall below 80 percent of the baseline. The investigation of work practices shall include a review of the safety equipment used and its condition; and the employee's work practices which included employee sanitation, pesticide handling procedures, and equipment usage. The employer shall maintain a written record of the findings, any changes in equipment or procedures, and any recommendations made to the employee.

(e) The employer shall remove an employee from exposure to organophosphate or carbamate pesticides if the employee's plasma cholinesterase level falls to 60 percent or less of baseline, or if red cell cholinesterase falls to 70 percent or less of baseline. The employee shall be removed from further exposure until cholinesterase values return to 80 percent or more of their respective baseline values. The employer shall maintain written records of the dates of removal and the dates when employees are returned to exposure.

(f) To meet the requirements of these regulations, acetylcholinesterase (also known as red blood cell cholinesterase) and butyrylcholinesterase (also known as plasma or serum cholinesterase or pseudocholinesterase) tests ordered by a medical supervisor for occupational health surveillance shall be performed by a clinical laboratory currently approved by the State Department of Health Services to perform these tests. By January 1, 2000, tests shall be performed according to the procedures outlined below. If tests cannot be performed according to the following procedures, the conversion procedure outlined in 3CCR §6728 (f)(8) shall be performed.

(1) Using personnel and procedures acceptable to the Department of Health Services (Business and Professions Code sections 1242,1243,1246,1269,2070; Health and Safety Code sections 120580, 1607), blood collection and storage shall be done according to the following conditions:

(A) Blood samples shall be kept in ice or at a temperature of 4º C until time of assay. If the sample is centrifuged to remove the erythrocytes from the plasma, the plasma shall be stored frozen at a temperature of minus 20º C until the assay is performed. If possible, the assay shall be performed within 24 hours after blood collection. Time of sample collection, analysis, and storage conditions shall be specified on the report.
(B) Ethylenediaminetetraacetic acid (EDTA) or heparin shall be used as an anticoagulant in a standard vacutainer tube.

(2) The reagents and equipment shall conform to the following conditions:

(A) A spectrophotometer at a wavelength between 405 and 425 nanometers shall be used.
(B) The assay shall be performed at a temperature of 25º C.
(C) The following conditions regarding the buffer/chromogen shall apply:
1. A sodium phosphate buffer shall be used at a concentration of 0.1 M adjusted to a pH of 8.0 with a pH meter calibrated at both 7.0 and 10.0.
2. Dithiobisnitrobenzoic acid (DTNB) at a stock concentration of 9.7 mM in 0.1 M sodium phosphate buffer pH 7.0 shall be used.
(D) The substrate acetylthiocholine iodide shall be used at a stock concentration of 10.1 mM in 0.1 M sodium phosphate buffer pH 8.0.
(E) The butyrylcholinesterase inhibitor quinidine hydrochloride monohydrate shall be used at a stock concentration of 6 mM in distilled deionized water.

(3) The acetylcholinesterase enzyme assay shall be performed within 15 minutes of preparation and the procedure for performing the assay shall be as follows:
(A) Measure 0.2 mL whole blood and add into a 1.8 mL solution of deionized distilled water; mix thoroughly and keep the solution on ice.
(B) To 2.5 mL of the sodium phosphate buffer, add 0.02 mL of the blood solution, 0.1 mL of DTNB (0.32 mM final concentration) and 0.1 mL of quinidine (0.2 mM final concentration); mix thoroughly and allow to sit for 5 minutes.
(C) Add 0.3 mL acetylthiocholine iodide (1.0 mM final concentration) into the buffer/sample solution and mix thoroughly.
(D) Measure absorbance over the linear portion of the enzyme activity curve in the spectrophotometer.

(4) The procedure for performing butyrylcholinesterase enzyme assay determination shall be as follows:
(A) Physical separation of plasma or serum shall be performed.
(B) If samples are frozen, they shall be thawed at room temperature to assure homogeneity of the sample.
(C) To 2.6 mL of the sodium phosphate buffer, add 0.02 mL of the plasma or serum and 0.1 mL of DTNB (0.32 mM final concentration), mix thoroughly and allow to sit for 5 minutes.
(D) Add 0.3 mL acetylthiocholine iodide (1.0 mM final concentration) into the buffer/sample solution and mix thoroughly.
(E) Measure absorbance over the linear portion of the enzyme activity curve in the spectrophotometer.

(5) A Buffer Blank containing 2.6 mL of sodium phosphate buffer, 0.3 mL of acetylthiocholine (1.0 mM final concentration), and 0.1 mL of DTNB (0.32 mM final concentration) and 0.02 mL of distilled deionized water shall be run with every batch of assays.

(6) Reporting units shall be in International Units per milliliter of sample (IU/mL).

(7) Baseline and follow up assays specified in 3CCR §6728 (c)(2)(A) shall be conducted by the same laboratory method.

(8) If an assay different from that described above is used, the method shall be shown comparable with the foregoing conditions and a conversion equation prepared. Results shall be reported in International Units per mL on both the original and the converted scale. The conditions to establish comparability shall be as described below.

(A) Using personnel and procedures acceptable to the Department of Health Services (Business and Professions Code sections 1242,1243,1246,1269,2070; Health and Safety Code sections 120580, 1607), blood samples shall be collected from at least ten subjects.

(B) Blood from each subject shall be tested by serial dilution as specified in "Comparison of Acetylcholinesterase Assays Run under Conditions Specified by the Standard Ellman Method and Conditions Specified by a Commercial Cholinesterase Reagent Kit." HS-1752, July 30, 1998, Department of Pesticide Regulation, Worker Health and Safety Branch.

(C) Test dilutions shall be made at 100% and 50% of enzyme activity.

(D) Triplicate samples shall be run by both the reference and the alternative methods.

E) Pearson product-moment correlation coefficient squared (r^2) shall be at least 0.9 between results of the alternative and reference methods.

Note: Authority cited: section 12981, Food and Agricultural Code.

Reference: Sections 12980 and 12981, Food and Agricultural Code.

Appendix A: Background

2. California Health and Safety Code section 105206

(a) A laboratory that performs cholinesterase testing on human blood drawn in California for an employer to enable the employer to satisfy his or her responsibilities for medical supervision of his or her employees who regularly handle pesticides pursuant to section 6728 of Title 3 of the California Code of Regulations or to respond to alleged exposure to cholinesterase inhibitors or known exposure to cholinesterase inhibitors that resulted in illness shall report the information specified in subdivision (b) to the Department of Pesticide Regulation. Reports shall be submitted to the Department of Pesticide Regulation on, at a minimum, a monthly basis. For the purpose of meeting the requirements in subdivision (d), the reports shall be submitted via electronic media and formatted in a manner approved by the director. The Department of Pesticide Regulation shall share information from cholinesterase reports with the OEHHA and the State Department of Public Health on an ongoing basis, in an electronic format, for the purpose of meeting the requirements of subdivisions (e) and (f).

(b) The testing laboratory shall report all of the following information in its possession in complying with subdivision (a):

(1) The test results in International Units per milliliter of sample (IU/mL).
(2) The purpose of the test, including baseline or other periodic testing, pursuant to the requirements of section 6728 of Title 3 of the California Code of Regulations, or evaluation of suspected pesticide illness.
(3) The name of the person tested.
(4) The date of birth of the person tested.
(5) The name, address, and telephone number of the health care provider or medical supervisor who ordered the analysis.
(6) The name, address, and telephone number of the analyzing laboratory.
(7) The accession number of the specimen.
(8) The date that the sample was collected from the patient and the date the result was reported.
(9) Contact information for the person tested and his or her employer, if known and readily available.

(c) The medical supervisor ordering the test for a person pursuant to subdivision (a) shall note in the test order the purpose of the test, pursuant to paragraph (2) of subdivision (b), and ensure that the person tested receives a copy of the cholinesterase test results and any recommendations from the medical supervisor within 14 days of the medical supervisor receiving the results.

(d) All information reported pursuant to this section shall be confidential, as provided in Section 100330, except that the OEHHA, the Department of Pesticide Regulation, and the State Department of Public Health may share the information for the purpose of surveillance, case management, investigation, environmental remediation, or abatement with the appropriate county agricultural commissioner and local health officer.

(e) The OEHHA shall review the cholinesterase test results and may provide an appropriate medical or toxicological consultation to the medical supervisor. In addition to the duties performed pursuant to section 105210, the OEHHA, in consultation with the Department of

Pesticide Regulation and the local health officer, may provide medical and toxicological consultation, as appropriate, to the county agricultural commissioner to address medical issues related to the investigation of cholinesterase inhibitor-related illness.

(f) By December 31, 2015, the Department of Pesticide Regulation and the OEHHA, in consultation with the State Department of Public Health, shall prepare a report on the effectiveness of the medical supervision program and the utility of laboratory-based reporting of cholinesterase testing for illness surveillance and prevention. The joint report may include recommendations to the Legislature that the Department of Pesticide Regulation and the OEHHA deem necessary. The Department of Pesticide Regulation and the OEHHA shall make the report publicly available on their Internet Web sites.

(g) This section shall remain in effect only until January 1, 2017, and as of that date is repealed, unless a later enacted statute, that is enacted before January 1, 2017, deletes or extends that date.

(Added by Stats. 2010, Ch. 369, Sec. 2. Effective January 1, 2011. Repealed as of January 1, 2017, by its own provisions.)

Appendix A: Background

3. Organophosphate and Carbamate Pesticides Mode of Action

Although organophosphates (OPs) and N-methyl carbamates (CBs) are two distinct chemical classes of insecticides, they have a common mechanism of action.

Mode of action

OPs and CBs are designed to inhibit the normal breakdown of Acetylcholine (ACh). ACh is a neurotransmitter, a chemical produced by a neuron that transmits signals from that neuron to another neuron, an exocrine gland, or a muscle. ACh is released in the junction between the two nerve cells (synapse) where it binds to its receptor on the target cell, inducing its activation and relaying the signal. Acetylcholinesterase (AChE) is an enzyme located in the intercellular space that is responsible for ACh degradation (Figure A3a). OPs and CBs act by occupying and blocking the site where the neurotransmitter attaches to the ChE enzyme. This leads to the buildup of ACh and continuous stimulation of the receptors on the target cells.

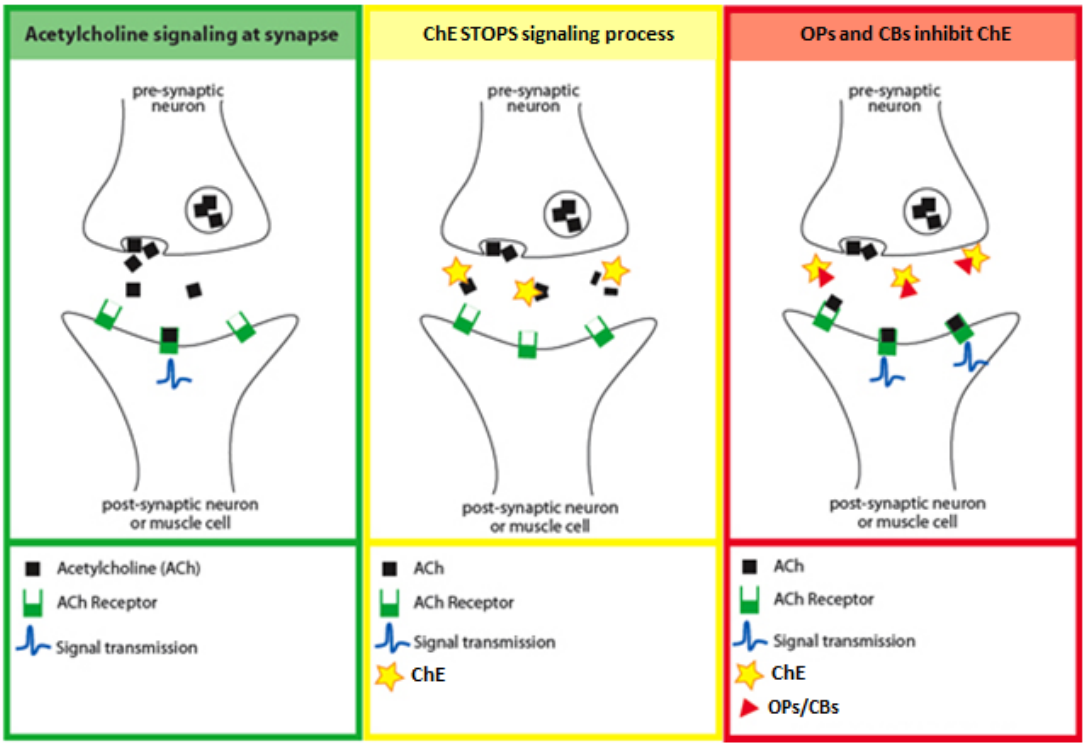


Figure A3a: *Mode of action of OPs and CBs on ChE and nerve signal transmission. (Modified from http://depts.washington.edu/opchild/acute.html.)*

Health effects and toxicity in humans

In humans, ACh plays a vital role in the central and peripheral nervous systems, including contraction of skeletal muscles, regulation of heart and respiratory rates, stimulation of gastrointestinal motility, and many other functions. OPs and CBs inhibit ChE activity resulting in overstimulation of the neurons due to accumulation of ACh at the neuronal junction. Compared to OPs, CBs have a shorter duration of action and generally, a lower toxicity.

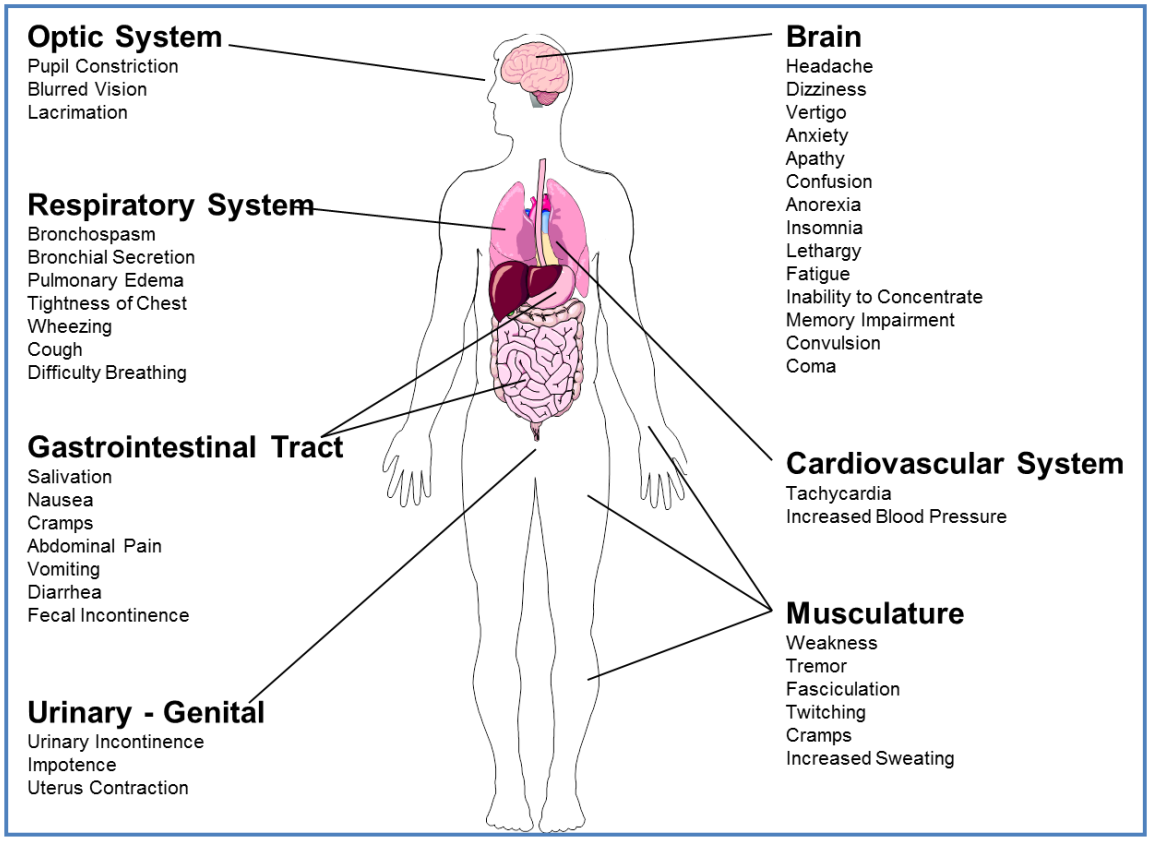


Figure A3b: *Most common signs and symptoms of OP and CB toxicity. (From presentation by Mohamed B. Abou-Donia)*

The most common signs and symptoms of acute OP/CB toxicity are slow heart rate, low blood pressure, difficulty breathing, salivation, lacrimation, sweating, abdominal pain, loose stools, muscle weakness, anxiety, and confusion (Figure A3b). Death is usually due to respiratory failure. Signs and symptoms vary with individual age and weight, compound, dose and route of exposure.

The EPA established four toxicity categories for acute hazards of pesticide products. Carbamate and organophosphate insecticides fall into all four categories (Table A3a).

Table A3a: US EPA pesticides toxicity categories

Categories	Toxicity	Rat Oral LD_{50}	Label
Category I	highly	< 50 mg/kg	Danger
Category II	moderately	50-500 mg/kg	Warning
Category III	low	500-5000 mg/kg	Caution
Category IV	very low	>5000 mg/kg	Not required

Appendix A: Background

4. Summary of Published Peer-Reviewed Literature of the Medical Supervisor Program

California's medical supervision program, as described in 3CCR §6728, has been previously reviewed. The following is a summary of selected articles evaluating the program:

- Coye *et al.* (1986) discussed the need to establish standards for agricultural workers exposed to OPs/CBs nationally and used the California medical supervision program as an example. The authors reviewed the use of biologic monitoring of agricultural workers to measure ChE activity, one of which was a colorimetric method (Ellman), the current standard[1].

- Ames *et al.* (1989) requested medical supervision records from physicians, laboratories and employers for the first 9 months in 1985. The authors also requested from the employers a list of pesticides used by employees whose ChE levels were below the "State thresholds."
  - Records from 542 agricultural workers that had at least one pre-exposure (baseline) and one post-exposure (periodic) ChE testing were analyzed.
  - At the time of this study, the State thresholds to remove workers from handling OPs/CBs were 60% or less of baseline for RBC ChE or 50% or less of baseline for plasma ChE.
  - In their analysis, 26 (4.8%) workers had ChE levels below the State threshold.
    - Eight workers were removed from work because of low ChE level.
    - **No actions were taken** for six workers because their ChE levels were within the laboratory's "normal range" even though the depressions exceed the State threshold.
    - Eight workers were tested because they were already ill from a pesticide exposure.
  - Their analysis indicated that the State thresholds at that time were set too high to prevent pesticide poisoning.
  - The authors reiterated the need to establish a baseline for each individual as there were nine workers whose ChE test results were below the State threshold but were within the laboratory "normal range" values.

- Ames *et al* (1989) published a companion article explaining the reason for the change in the California regulation in 1988 which changed the "action" threshold from 60% to 70% depression of RBC ChE activity and from 50% to 60% depression of plasma ChE activity.
  - The new levels were in line with the thresholds recommended by the World Health Organization.
  - The authors also reviewed problems with the medical supervision program and made recommendations for improvement.
    - Exposure for Program requirement – change from 30 hours in 30 days to more than six days in any 30-day period.[1] No reason was given for selecting six days as the "trigger."
    - Mandate frequency of ChE tests by state code– every 30 days for first 3 tests, then every 60 days or as specified by the medical supervisor. [1]
    - Require employers to inform CAC of the name of their medical supervisor.[1]

[1] Adopted in current regulations.

- Increase county enforcement of Program requirements.
- Use of a single analytical test method and standardization of test methodology.
- State certification of laboratories that perform ChE analysis.[2]
- Require employers to inform physician of pesticide exposure status to determine if test is for baseline or periodic testing.
- Increase physician education of the Program and revise the *Guidelines for Physicians*.[3]

- Brown *et al.* (1989) reviewed data for occupational illnesses from OPs/CBs among agricultural applicators in California between 1982 and 1985 (n=238).
  - The authors classified the exposures into five categories: chronic, short-term, accident, safety violation, and weather.
  - They concluded that counties need to include ChE monitoring results in their investigation to assist in establishing ChE inhibition and illness.
  - They also suggested that careful ChE monitoring may reduce the likelihood that persons receiving a single massive dose of OPs/CBs will develop clinical illness.

- Fillmore and Lessenger (1993) published their findings from a 1989 to 1990 retrospective cohort study of 155 employees who had ChE baselines established.
  - Only 79 of the 155 workers had ongoing ChE monitoring.
  - The authors indicated that conducting a ChE monitoring program is far more complicated than just measuring laboratory values.
  - Further, they stressed that careful attention must be paid to comparing ChE values to previous ChE test results and baselines.
  - They also identified a need for regulations to clearly indicate the testing frequency for monitoring, "especially during peak spraying periods."
  - They suggested program improvements and better enforcement of regulations.

- Ames and Menendez (2001) conducted a survey of "medical supervisors of record" in 1992.
  - The survey, based on 101 responses, indicated that medical supervisors were supportive of the Program and felt that it was effective in preventing pesticide poisoning.
  - The survey focused on the medical supervisor responsibilities and did not address the employer requirements of the program.

- Wilson *et al.* (2004) determined that commonly used clinical ChE kits (standard Ellman) were not optimal for assaying blood ChE.
  - This study led, in part, to the revision of 3 CCR §6728(f) to specify the use of the Modified Ellman method for RBC and plasma ChE activity measurement.[1]
  - The authors performed a validation study of ChE activity measurements, and the results were used, in part, for the Department of Health Services to approve nine clinical laboratories for ChE testing.

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2 Laboratories are currently approved by CDPH but not certified.

3 Ongoing

Appendix A: Background

5. Comparison of Washington and California's Cholinesterase Results Reporting Program

Both California and Washington have a ChE test results reporting requirement and comparisons are inevitable. Although Washington's program was patterned after California's Medical Supervision program, there are some inherent differences in the ChE results reporting structure of the two states:

- California's ChE results reporting program is governed by the DPR and data is shared with the OEHHA. Washington's program is under the Department of Labor and Industries, Division of Occupational Safety and Health (DOSH).

- In California, any worker who regularly handles (more than six days in a 30-day period) organophosphate or carbamate pesticides with the signal word DANGER" or "WARNING" is required to be part of the medical supervision program. Employees who work only with closed systems are required, at a minimum, to have a baseline ChE determination. In Washington, the handling threshold is 30 or more hours in any 30-day period. Hours spent mixing/loading using closed systems are not considered when calculating the handling threshold for the purposes of periodic monitoring. Employers are not required to offer ChE testing to workers who only handle carbamates.

- Washington conducted extensive outreach and training with a) healthcare providers, b) employers and c) employees prior to the actual implementation of the program.

- Washington allows workers to decline participation in their medical supervision program only after they have been trained on the program and they have consulted with a medical provider. An employer who discourages participation in ChE monitoring, or in any way interferes with an employee's decision to continue with the program may represent unlawful discrimination under Washington state regulations.

- Washington's employers are reimbursed by DOSH for testing services and administrative costs.

- Washington does not hold healthcare providers responsible for ensuring employer and employee compliance with the rule, but may cite employers for non-compliance of the rule in accordance with state regulations. (Furman, 2010).

- In California, covered employees are required to have baseline red blood cell (RBC) and plasma ChE determinations which are verified every two years. Washington requires that the baseline be determined annually.

- Currently, there are six laboratories in California approved to perform ChE analysis for occupational health surveillance. In Washington, all specimen samples are sent to one laboratory. This laboratory assesses the adequacy of the sample upon receipt, and notifies the provider if the sample is not adequate. A quantitative enzymatic assay is used to measure ChE activity which includes the Ellman standard for RBC and plasma (http://etd.paml.com/etd/display.php?id=504).

- In California, employers who have an employee who regularly handles cholinesterase-inhibiting pesticides are required to have a written agreement signed by a physician, and the employer responsible for the employees. The agreement should state that the physician has agreed to provide medical supervision. The employer submits a copy of this agreement to their County Agricultural Commissioner no later than when an employee begins to regularly handle pesticides. In Washington, the Department of Labor and Industries maintains an online list of registered healthcare providers who can serve as medical supervisor.

- California regulations require that an employer maintains records of his employee's blood test results, and medical supervisor's advice for 3 years (3CCR §6728 Section (c)(3)), while Washington requires that employers maintain medical monitoring and other records for 7 years (WAC 296-307-14835).

- The responsibilities of the employer in California's Medical Supervision Program include keeping a record of the written agreement with a physician for medical supervision, posting the name, address and phone number of the medical supervisor in a prominent place, keeping the medical supervisor's recommendations on record, following the recommendations of medical supervisor, investigating the work practices of employees whose ChE levels fall below 80%, relieving an employee from his pesticide handling duties if ChE levels are below the action levels, and maintaining the records of investigation/changes made. In addition to these responsibilities, Washington requires that employers report the number of hours an employee handled pesticides to the medical provider with each periodic test.

- Although California's HSC §105206 states that the medical supervisor should ensure that the person tested receives a copy of the ChE test results and any recommendations from the medical supervisor within 14 days of the medical supervisor receiving the results, 3CCR §6728 does not specify how information transfer occurs other than the "employer shall follow the recommendations of the medical supervisor concerning matters of occupational health." On the other hand, in addition to sending the test results to DOSH, Washington specifies that test results go to the doctor who interprets the results and provides his recommendations to the employer (Washington Department of Labor and Industries (a), 2006). In 2006, the rule was amended to require employers to obtain a written recommendation from the healthcare provider for each employee test (including the baselines) and evaluation, and provide a copy of the recommendation to the employee, either directly or through the health care provider, within 5 days of receipt (Washington Department of Labor and Industries (b), 2006). In their "Information for Farm Workers" fact sheet, it also states the doctor will send a report to a worker's employer telling him that the worker has had a test, and what the results mean. The employer is responsible for making sure that the worker receives a copy of the doctor's report, and if a worker's ChE level drops more than 20%, the employer will review the worker's work activities to determine the problem. If needed, the worker is removed from working with ChE-inhibiting pesticides (Washington Department of Labor and Industries (c), 2006).

Appendix B: LABORATORY-BASED REPORTING OF CHOLINESTERASE TESTING

1. Structure of California's Medical Supervision Program

The Program's goals are to monitor agricultural pesticide handlers through periodic measurements of their red blood cell (RBC) and plasma ChE activity, and to identify and prevent exposure resulting in illness/injury of employees who regularly handle OPs/CBs more than six days in a 30-day period.

The Program requires an employer to contract a licensed physician to act as a medical supervisor (Figure B1a (1)). Employers are required to provide the local County Agricultural Commissioner's office with a copy of this contract (Figure B1a (2)). A medical supervisor monitors the ChE activity levels of handlers to ensure their safety. The Program also requires that a medical supervisor possess a copy of, and be aware of, the contents of the *Guidelines for Physicians*. The medical supervisor must also order tests for baseline levels of RBC and plasma ChE performed by a laboratory (Figure B1a (3)). Testing should be conducted before a worker begins handling OPs/CBs. Routine monitoring of RBC and plasma ChE levels of the workers who regularly handle OPs/CBs are required. The medical supervisor compares the routine monitoring test results to the baseline levels to evaluate ChE depression and makes recommendations, based on these results, to the employer. These recommendations may include allowing a worker to continue working with OPs/CBs, re-evaluation of work place practices, or temporarily removing the worker from handling such pesticides.

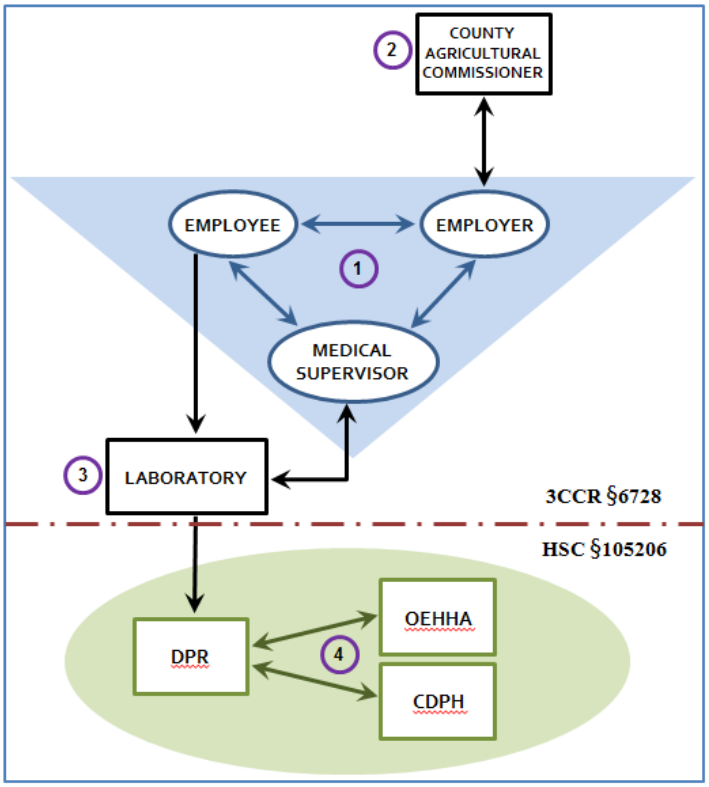


Figure B1a: *Framework of the Medical Supervision Program.*

The Guidelines for Physicians who supervise workers exposed to cholinesterase-inhibiting pesticides (https://oehha.ca.gov/media/downloads/pesticides/document-pesticides/physicianguidelines.pdf).

The *Guidelines for Physicians* specifies recommendations on baseline ChE level calculation, frequency of tests, and interpretation of the test results.

Calculation of the baseline – The baseline is calculated by averaging two tests collected at least 72 hours and less than 14 days apart when a worker has not handled OPs/CBs for at least 30 days. Baselines are required to be verified at least once every two years. If two baseline

tests differ by more than 15%, a third test should be performed and the average of the two closest results should be used as an estimate of baseline ChE level.

Routine monitoring – Routine testing is required of handlers who work with OPs/CBs for more than six days in any 30-day period, beginning with the first day of handling. For additional requirements for periodic testing see Figure B1b.

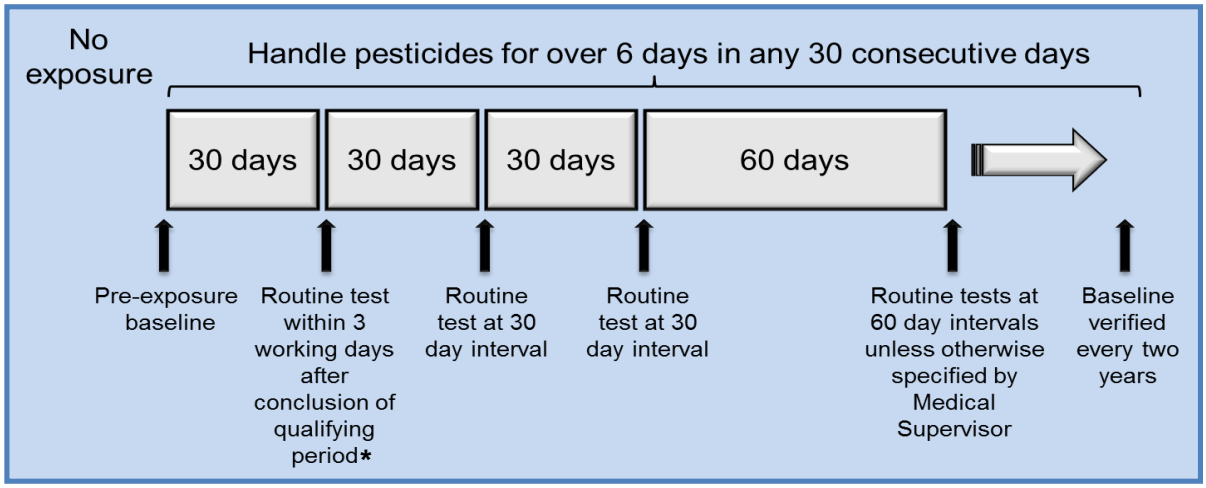


Figure B1b: *Summary diagram on the frequency of ChE activity testing.*
** –Qualifying period: The 30 consecutive day period during employees handle OPs/CBs for more than six days.*

Interpretation of the test results – To assess the degree of RBC and plasma ChE depression, the medical supervisor should calculate the percent change of periodic test results from baseline values. An 80% decline from baseline of either RBC or plasma ChE indicates a need for an investigation of workplace practices (e.g., safety protocols, potential sources of exposure), as well as prompt retesting of the worker. If a worker's ChE value is below 70% of RBC baseline or below 60% of plasma baseline, he/she must be removed from further exposure. The *Guidelines for Physicians* specifies repeated testing until ChE levels return to 80% or greater of baseline.

Appendix B: LABORATORY-BASED REPORTING OF CHOLINESTERASE TESTING

2. Evaluation of the Process of Laboratory-Based Reporting

A. Laboratories approved for cholinesterase testing for occupational health surveillance

The Program requires that ChE tests ordered by medical supervisors shall be performed by a clinical laboratory approved by the State Department of Health Services (SDHS). On July 1, 2007, SB 162 (California Public Health Act) established the California Department of Public Health (CDPH) and transferred certain programs from SDHS to CDPH. CDPH is responsible for maintaining the list of laboratories approved for ChE testing for occupational health surveillance (see page 48). A laboratory is approved to perform ChE tests if it complies with the use of the prescribed methods for their analysis (e.g., Ellman method), or a method approved by CDPH. The procedure for blood collection and storage, as well as the method for analysis, are outlined in 3CCR §6728 (Appendix A1).

In 2010, only six of the 13 laboratories on CDPH's list at that time confirmed that they still perform ChE analysis for occupational health surveillance (Table B2a). To the best of our knowledge, these laboratories do not go through proficiency assessments for ChE testing. Laboratories that perform similar analytical tests usually undergo regular evaluations by an independent 3rd party to ensure the quality and validity of their test methods.

Table B2a: Laboratories that perform cholinesterase test analysis	
ARUP	ARUP Laboratories, Salt Lake City, UT
MEDTOX	MEDTOX Laboratories Inc., St. Paul, MN
PACTOX	Pacific Toxicology Laboratory, Chatsworth, CA
PALI	Physicians Automated Laboratory, Inc., Bakersfield, CA
QDI- SAC	Quest Diagnostics Inc., Sacramento, CA
QDI- SJC	Quest Diagnostics Inc., Nichols Institute, San Juan Capistrano, CA

B. The roles and responsibilities of a medical supervisor

In addition to ordering the RBC and plasma ChE tests, a medical supervisor is also responsible for interpreting the results and making recommendations to ensure the safety of handlers as defined in the Program and HSC §105206. A more detailed description of the roles and responsibilities of a medical supervisor can be found in the *Guidelines for Physicians*.

C. Obtaining a blood specimen and transfer of data for cholinesterase testing

An employer sends an employee under the Program for ChE testing to a contracted medical supervisor who will order the ChE tests. The employee's blood is drawn at the medical supervisor's office or at a drawing laboratory. If the blood specimen is drawn at a physician's office or at a drawing laboratory that is not equipped to analyze ChE tests, the specimen is forwarded to a *reference laboratory* for analysis.

Any information indicated by the medical supervisor on a test order is recorded by the drawing laboratory and transmitted to the reference laboratory. The ChE test orders may contain missing or incomplete information on the employee, the ordering physician, or the employer (e.g. information left blank, partially completed or entered as "unavailable," missing first or last names, etc.). However, even though the ChE test order may not contain all the information required by HSC §105206, it does not prevent the ordering physician from submitting the test order.

The reference laboratories have little or no direct communication with the tested employee or ordering physician. These laboratories can submit to DPR only the information that have been provided to them and may not have, or are not able to obtain, the HSC §105206-specified data elements that are required in the ChE test reports.

The 6 laboratories submit ChE test results to DPR on, at a minimum, a monthly basis.

D. Reporting of cholinesterase test results to DPR

DPR modified its Secure Access Website (SAW) to develop a mechanism for electronic reporting. SAW is an online application used by DPR to transmit documents containing personal and confidential information related to pesticide illness investigations. SAW uses SSL (Secure Socket Layer) to encrypt network communication from a user to DPR. Microsoft Excel was chosen as the standard for submitting ChE test reports with each column header in the spreadsheet representing a data element. Laboratories are responsible for generating these Excel spreadsheets. We are unable to implement quality control measures on the submitted reports through data validation rules. Occasionally, the laboratories deviate from the prescribed reporting format.

Table B2b: Data Elements specified under HSC §105206	
1.	RESULTS of the ChE test in IU/mL
2.	PURPOSE of the test
3.	NAME of person tested
4.	DATE OF BIRTH of person tested
5.	NAME, ADDRESS and TELEPHONE NUMBER of medical supervisor who ordered the analysis
6.	NAME, ADDRESS, TELEPHONE of the analyzing laboratory
7.	ACCESSION NUMBER of the specimen
8.	COLLECTION DATE when blood specimen was drawn
9.	RESULT REPORT DATE
10.	PATIENT'S contact information
11.	EMPLOYER'S contact information (if known and readily available

In addition to the data elements specified under HSC §105206 (Table B2b), DPR requested additional information be included in the ChE test reports to assist in identifying unique patient records and rule out ChE tests not related to the Program (Table B2c).

Table B2c: Additional data elements requested by DPR	
1.	TEST TYPE – ChE RBC (Acetylcholinesterase) and ChE Plasma (Serum or Butyrylcholinesterase). Both test types are required for persons being tested for blood ChE in the Program.
2.	LOWER and UPPER LIMIT OF NORMAL RANGE – The reference range of normal ChE values vary amongst laboratories.
3.	DATE OF RECEIPT BY LABORATORY – when a reference laboratory received the blood specimen sample
4.	ANALYSIS DATE – when the blood specimen was processed using the prescribed analytic method (e.g., Ellman method)
5.	Drawing Laboratory's Name, Address, Telephone, Fax, Cellular Number, Email
6.	Medical supervisor's middle initial, fax number and email
7.	Employer's fax number, and email.

E. Purpose of Cholinesterase Test

Early in discussions with DPR, the laboratories communicated their concerns about meeting the requirements of HSC §105206. The laboratories stated that they may not be able to report the purpose of the tests since ordering physicians do not indicate this on the laboratory requisition slips. Without knowing the reason for the ChE test, it is difficult to interpret the test result in relation to the worker's activities and practices. Furthermore, this information is critical for accurately calculating the percent ChE depression of a worker.

Purpose of Test Terminology

- **BASELINE**: Pre-exposure test ordered to establish the normal ChE activity level of a worker under the Program.
- **ROUTINE MONITORING**: Test ordered for routine monitoring of a worker under medical supervision.
- **EVENT (Evaluation of suspected illness)**: Test ordered to identify effects of a suspected or reported pesticide exposure.

Early ChE test reports showed that there was no standard terminology used by physicians to indicate the purpose of the test. In 2011, DPR and OEHHA jointly sent a letter to 841[1] healthcare providers and/or drawing laboratories in an effort to improve the data quality of the reported ChE results (see page 51). The letter explained the requirements of HSC §105206 and the responsibilities of a medical supervisor in fulfilling these requirements. The reference laboratories were provided with the standard terminology for ChE reporting and were asked to disseminate this information to their clients (ordering physicians and drawing

[1] Total number of names of doctors and/or laboratories entered as "ordering physicians" on the 2011 ChE test reports.

laboratories). Some laboratories have made efforts to capture this information by modifying their requisition slips, or by contacting the medical supervisors' offices. To date, the true purpose of a ChE test or whether the test results were part of the Program remains unclear (Table B2d).

Table B2d: *Summary of Concerns/Issues Regarding the "Purpose of Test"*

Concerns/Issues	Action Taken	Status
• Physicians do not provide the laboratories the purpose of the test at time of order submission.	• 2011 – DPR and OEHHA jointly sent outreach letters to physicians reminding them to enter the purpose when ordering ChE tests. • OEHHA outreach to medical supervisors.	• Unresolved. • OEHHA's outreach efforts ongoing.
• Ambiguous purpose of test. Examples: "Close Contact," "989.9," "Annual Routine," "Blueprint for Wellness," "CA-Required," "CA Patient," "Draw 1," "HazMat," "ChE," etc.	• Discussed with the laboratories. • OEHHA outreach to medical supervisors.	• Unresolved. • OEHHA's outreach efforts ongoing.
• Laboratories are not able to provide the true purpose of the test (as it relates to the Program) in their reports.	• 2011 – DPR instructed laboratories to include the "purpose of test" in the reports • 2012 – DPR provided the laboratories with standard terminology to use in their reports for the purpose of the test.	• 2013-2014 – Two laboratories created "ask and order" entry online ordering systems. • Two laboratories pre-printed "purpose of test" options on their requisition slips. • Other reference laboratories have the ability to modify their Laboratory Information Systems (LIS) to capture the purpose of the ChE test. However, modifying a laboratory's LIS to capture the purpose of the test is not specified in the HSC §105206. • Unresolved.

B. Cholinesterase Data Acquisition and Clean-up

Laboratories transmit ChE test results through secure portals – four through DPR's SAW and two through the laboratories' own websites. The latter requires DPR to perform additional steps to obtain these reports.

A major challenge to effectively interpret the ChE monitoring data has been the missing and incorrect data reported by the laboratories. Without this information, we are unable to follow-up with the employers when the employee's ChE test results require action (see Table 1 for action levels of RBC and plasma ChE and the associated actions required under the Program).

Once the electronic files are received, staff manually review data and correct misspelled names, reconcile variations in the spelling of names when all other fields are the same, and reconcile birth dates for paired samples (e.g., 01/01/1991 for the RBC ChE test and 07/01/1991 for the plasma ChE test of the same person). DPR scientists seek clarification from the reporting laboratory on issues such as illogical dates (i.e. 01/01/1900) or a large number of test results from a single laboratory that exceed their normal reference range values by a wide margin. We continue to work with the laboratories to ensure that they provide consistent and complete ChE test results to the extent possible. Concerns and issues regarding the data are summarized in Table B2e.

Table B2e: *Summary of Concerns and Issues Regarding the Data*

Concerns/Issues	Action Taken	Status
• Report format variation across laboratories.	• DPR provides guidance to laboratories on the specific Excel spreadsheet format.	• 2012 – All laboratories began using the standardized format. • 2015 – One laboratory temporarily submits reports in a non-standard format due to a change in their laboratory information system.
• Missing, partially completed or incorrectly entered data. Also entered as "unavailable."	• DPR informs laboratories of missing or incomplete data.	• Laboratories contend that they can only report information that is provided to them. • Unresolved.
• Duplicate test results.	• DPR informs laboratories of duplicate test results.	• Laboratories implemented changes to their Quality Assurance procedures resulting in fewer duplicate records.

Concerns/Issues	Action Taken	Status
• Variations in Normal Reference Range values among the laboratories. These values are laboratory-specific. • One laboratory uses gender-specific normal ranges for their plasma ChE test, and enters "Unavailable" in the reference range if the gender is unknown.	• Coordinating with CDPH to ensure consistency and reliability of the test results values.	• Unresolved.
• Data entry errors.	• DPR asks the laboratories to verify or correct the information on the report.	• Laboratories review reports prior to submitting, resulting in fewer data entry errors.
• One laboratory thought that the reporting requirement ended in 2013.	• 2014 - DPR contacted the laboratory to continue reporting.	• The laboratory resumed reporting.
• DPR receives ALL ChE test results in California.	• Laboratories provided guidance on some test results that can be definitively excluded (e.g., HazMat, DTSC, if the ChE test type was reported as a ratio).	• Unresolved.

Laboratories Approved for Cholinesterase Testing for Occupational Health Surveillance, January 1, 2007

State of California—Health and Human Services Agency
Department of Health Services

California Department of Health Services

ARNOLD SCHWARZENEGGER
Governor

This List Dated **January 1, 2007,** Replaces and Supersedes
The Previous List Dated June 1, 2006.

Laboratories Approved for Cholinesterase Testing for Occupational Health Surveillance
Reference: California Code of Regulations, Title 3, Section 6728(f)

LABORATORY	COUNTY	TESTING DONE ON-SITE	METHOD
	Kern		
Physicians Automated Laboratory, Inc. 2801 H Street Bakersfield, CA 93301 Attn: C. Bruce Smith Phone: (661) 325-0744 FAX: (661) 327-9163		Yes	Colorimetric
	Kings		
Corcoran District Hospital Laboratory 1310 Hanna Avenue Corcoran, CA 93212 Attn: Ron A. Bico Phone: (559) 992-5051, x351 FAX: (559) 992-3972		(a.)	
	Los Angeles		
Pacific Toxicology Laboratories 9348 De Soto Avenue Chatsworth, CA 91311 Attn: Donald R. Simpson, M.D. Phone: (818) 598-3110 FAX: (818) 598-3116		Yes	Colorimetric

Footnote (a.) Corcoran District Hospital Laboratory performs the plasma cholinesterase test on-site using a colorimetric method. The RBC test is referred to a different approved laboratory.

Environmental Health Laboratory Branch, 850 Marina Bay Parkway, G365, Richmond, CA 94804-6403
Phone: (510) 620-2801 Fax: (510) 620-2825
Internet Address: www.dhs.ca.gov/ehlb

Monterey

George L. Mee Memorial Hospital 300 Canal Street King City, CA 93930 Attn: Judy Antonio Phone: (831) 385-7212 FAX: (831) 385-5399	Yes	Colorimetric
Salinas Valley Primecare Medical Group 909 Blanco Circle Salinas, CA 93901 Attn: Gerald Oehler, MD Phone: (831) 751-7070	Yes	Colorimetric

Orange

Quest Diagnostics Incorporated Nichols Institute 33608 Ortega Highway San Juan Capistrano, CA 92690-6130 Attn: Sandy Burns Phone: (949) 728-4629 FAX: (949) 728-4860	Yes	Colorimetric
U.C. Irvine Medical Center Department of Pathology 101 City Drive South Orange, CA 92868 Attn: Steven Sarandis Phone: (714) 456-5293 FAX: (714) 456-2200	Yes	Colorimetric

Sacramento

Quest Diagnostics 3714 Northgate Boulevard Sacramento, CA 95834 Attn: Sue Aitken Phone: (916) 927-9900 FAX: (916) 564-0847	Yes	Colorimetric

Tulare

Sierra View District Outpatient Laboratory 263 N. Pearson, Suite 102 Porterville, CA 93257 Attn: Dave Workman Phone: (559) 784-7852 FAX: (559) 784-0614	Yes	Colorimetric

OUT OF STATE

Kansas

Quest Diagnostics 10101 Renner Blvd. Lenexa, KS 66219 Attn: P. Patrick James, M.D. Phone: (913) 888-1770 FAX: (913) 894-9029	Yes	Colorimetric
Clinical Reference Laboratory, Inc. 8433 Quivira Road Lenexa, KS 66215 Attn: Robert Stout, Ph.D. Phone: (913) 492-3652	Yes	Colorimetric

Minnesota

MEDTOX Laboratories, Inc. 402 West County Road D St Paul, MN 55112 Attn: Jennifer A. Collins, Ph.D. Phone: (651) 636-7466	Yes	Colorimetric

Utah

ARUP Laboratories 500 Chipeta Way Salt Lake City, UT 84108 Attn: Margo Taylor Phone: (801) 583-2787, x3100 FAX: (801) 584-5108	Yes	Colorimetric

Edmund G. Brown Jr.
Governor

December 21, 2011

<First name><Last name>, MD
<address>
<City>, California <zip>

RE: NEW REQUIREMENTS FOR PHYSICIANS WHO ORDER CHOLINESTERASE TESTS FOR THE MEDICAL SUPERVISION PROGRAM FOR AGRICULTURAL WORKERS EXPOSED TO CHOLINESTERASE-INHIBITING PESTICIDES

Dear Dr. <Last name>:

Effective January 1, 2011, physicians who order cholinesterase tests for the Medical Supervision Program for agricultural pesticide handlers exposed to cholinesterase-inhibiting pesticides must indicate the purpose of the test on the requisition form to the testing laboratory. This includes tests for establishing a baseline, for routine monitoring, or for evaluation of suspected pesticide illness. These requirements are specified in the newly adopted Section 105206, subsection (c) of the California Health and Safety Code.

In addition, the ordering physician must provide to the person tested a copy of the cholinesterase test results and any recommendations within 14 days of receiving the results.

The complete text of Section 105206 of the California Health and Safety Code is attached. This law came into existence in an effort to evaluate the effectiveness of the Medical Supervision Program for agricultural workers who regularly handle cholinesterase-inhibiting pesticides. The California Department of Pesticide Regulation (CDPR) and the Office of Environmental Health Hazard Assessment (OEHHA) are jointly responsible for the program evaluation. Your cooperation is crucial to this effort.

1001 I Street • P.O. Box 4015 • Sacramento, California 95812-4015 • www.cdpr.ca.gov

<First name><Last name>, MD
December 21, 2011
Page 2

If you are currently contracted with an employer as a medical supervisor under this program, you are already required to be aware of the contents of the Guidelines for Physicians Who Supervise Workers Exposed to Cholinesterase-Inhibiting Pesticides (4th Edition, 2002 available at: http://oehha.ca.gov/pesticides/pdf/docguide2002.pdf). In addition, there is an online training course on the Medical Supervision Program that awards free CME credits and can be viewed at: https://www.mededpesticide.org/. The course is suitable for a review of the program or for a physician just starting in the program.

If you have any questions on the new cholinesterase reporting requirements, please feel free to contact either of us.

Thank you for your attention.

Sincerely,

William Ngai, MD, MPH
OEHHA / Pesticide and
Environmental Toxicology Branch
(510) 622-3221
William.ngai@oehha.ca.gov

Saturnino Yanga, DVM, MVPH
CDPR / Worker Health and Safety Branch
(916) 445-6387
syanga@cdpr.ca.gov

Attachment

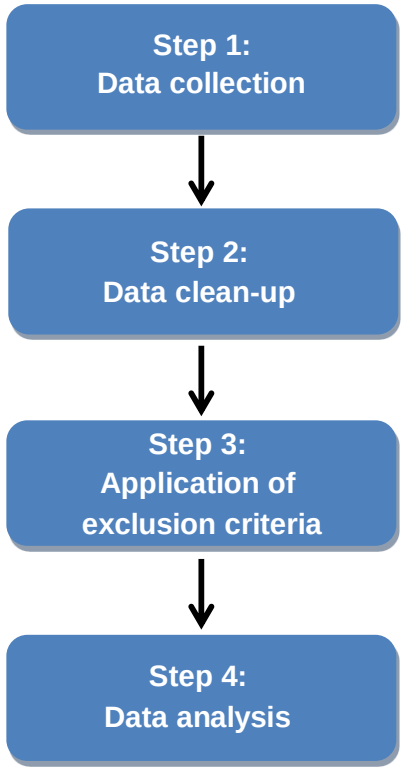
cc: Dr. Anna Fan, Chief, Pesticide Environmental Toxicology Branch, OEHHA/Oakland
Susan Edmiston, Environmental Program Manager II, WHS Branch, CDPR
George Farnsworth, Environmental Program Manger I, WHS Branch, CDPR

Appendix C: ELECTRONIC CHOLINESTERASE DATA ANALYSIS

HSC §105206, enacted in 2011, stipulated several changes in California's medical supervision program. The law requires certified laboratories that analyze the ChE activity in blood samples of employees who regularly handle OP/CB pesticides, to report specific information pertaining to the test result, the employee, his or her employer, his or her physician, and the laboratory to DPR. DPR shares this information with OEHHA and CDPH.

DPR worked with these laboratories to streamline the blood ChE reporting process. OEHHA analyzed the test results in order to evaluate the effectiveness of the Program and the utility of laboratory-based reporting, and to develop recommendations regarding continuation of the Program beyond the end of 2016. Figure C1 illustrates the four steps taken in data acquisition and analysis.

Figure C1: *Workflow for ChE Data Acquisition and Analysis*



Step 1: Data collection

Six laboratories are approved by CDPH for the analysis of ChE activity levels in blood specimens for occupational health surveillance, and each sends test results to DPR in Excel format on a monthly basis (at minimum). Figure C2 summarizes the number of records of ChE test results transmitted each year from 2011 through 2014 by the six laboratories.

One of the major challenges to effectively interpreting the ChE monitoring data was missing and incorrect data reported by the laboratories. DPR manually performed a first round of data clean-up, correcting misspelled names, reconciling variations in the spelling of names when all other fields were the same, and reconciling birth dates for paired samples (e.g., 01/01/1991 for the RBC ChE test and 07/01/1991 for the plasma ChE test for the same person). DPR also asked for clarification from the reporting laboratory when an entered date was not logical (i.e. 01/01/1900) or when test results from a single laboratory exceeded the normal range. DPR has been working with the laboratories to provide consistent, complete and accurate reporting of ChE testing results but these types of problems continue to exist.

Step 2: Data clean-up

OEHHA obtained the ChE data from DPR through a secure access website (SAW). Over 110,000 records were downloaded for the period of 2011-2014. To assure data consistency within each laboratory, OEHHA used SAS (Statistical Analysis System, software that manages data and performs statistical analyses) to further clean the data (e.g., reformatting the data, flagging missing information, removing duplicates, and correcting typographical errors).

After cleaning, data processing included selection of test results and application of exclusion criteria for analysis, estimation of baseline values, calculation of variation from baseline, and implementation of a screening tool to quickly identify cases of interest. The processed data were exported back into Excel format to be analyzed using both Excel and GIS (geographic information system) software.

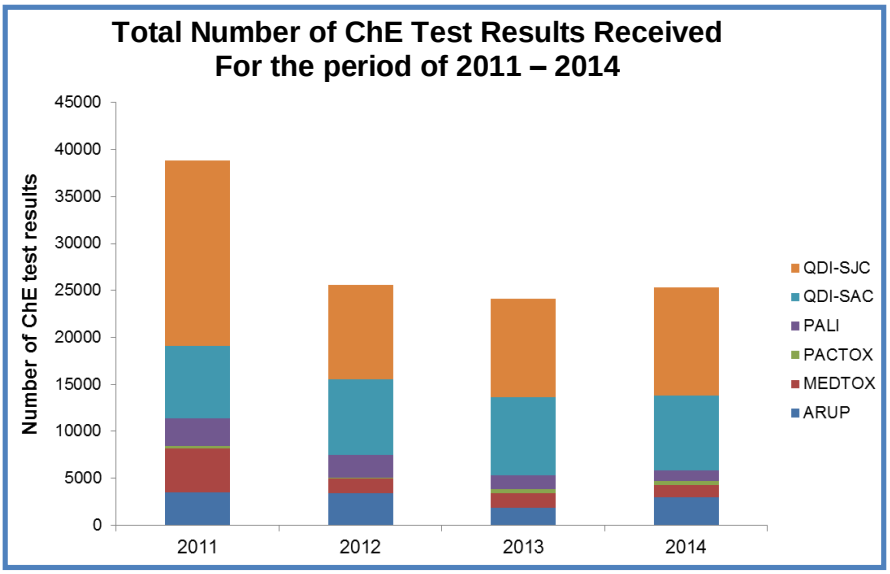


Figure C2: *Yearly number of ChE test results received by DPR from the 6 laboratories between 2011 and 2014. See Appendix B2 for complete laboratory names and locations.*

Step 3: Application of exclusion criteria

The laboratories reported all ChE test results to DPR, not just those related to the Program. As a result, OEHHA developed criteria for excluding irrelevant records from further analysis. Test results that fit any one of the following criteria were excluded from further analysis:

- Contained only RBC or plasma ChE activity levels, but not both
- Indicated employers that do not apply pesticides (e.g., California Department of Toxic Substance Control, San Francisco General Hospital)
- Showed that the age of the test subject was less than 16 or over 75 years old
- Showed that the physician who ordered the test was located outside California

In order to focus on records that were more likely to be related to the Program, tests were excluded from further analysis if they were ordered by a physician who did not order ChE tests for any other individuals from 2011-2013.

After application of our exclusion criteria there were 58,064 paired sample tests (RBC and plasma) for 11,735 apparent pesticide handlers. It should be noted that this process might have erroneously eliminated some data that were actually relevant to the Program or included some data that were not relevant to the Program.

In order to investigate the patterns of ChE activity level and the frequency of ChE depressions, we divided the dataset into two groups depending on whether individuals had more or less than two paired RBC and plasma ChE test results within any given year (Figure C3):

1. Individuals for whom a baseline was taken regularly (annually or every two years) but did not receive other periodic testing (follow-up).
2. Individuals for whom a baseline was taken regularly and received other routine periodic testing.

The second group was used for the analysis of individual ChE activity patterns, and frequency and type of depressions.

The histogram below shows a significant reduction in the number of ChE test results (Figure C4a) and number of individuals (Figure C4b) following the application of the exclusion criteria. The reduction is even more substantial when considering only individuals with periodic testing. This suggests that (1) a large number of ChE test results reported by the laboratories were not related to the Program, and (2) most individuals apparently in the Program (89%) did not have routine periodic testing. The apparent lack of longitudinal monitoring of individuals could be because (1) these individuals do not participate in the Program and the exclusion criteria failed to exclude them, (2) these individuals did not need to be tested more frequently because they did not handle pesticides more than six days per 30-day period, or (3) medical supervisors and/or employers failed to comply with the Program's requirements.

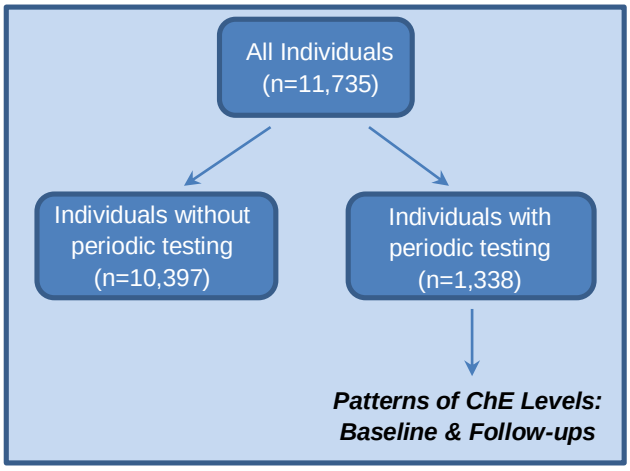


Figure C3: *Diagram of the dataset split in two groups for analysis. "Periodic testing" was defined as a record with more than two paired RBC and plasma ChE test results within any given year.*

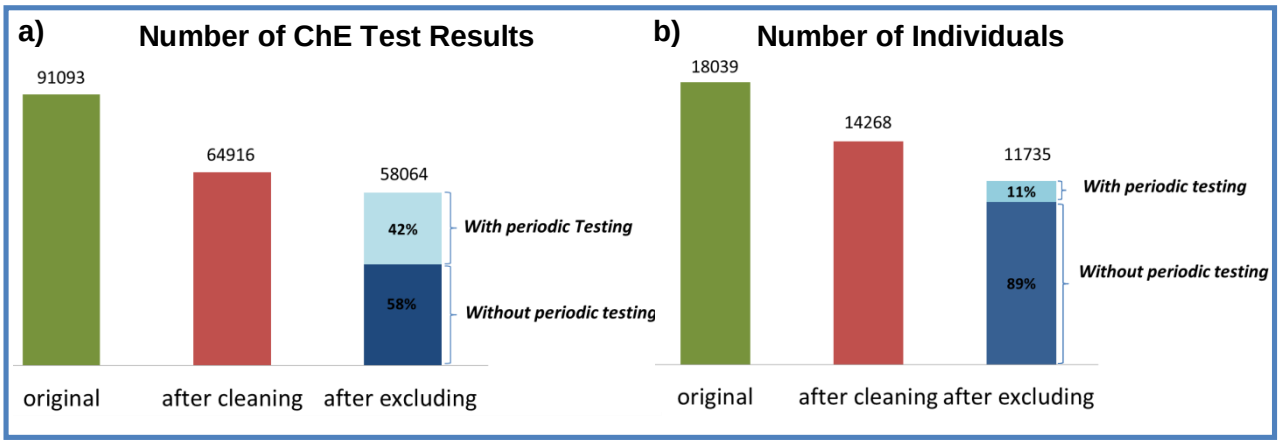
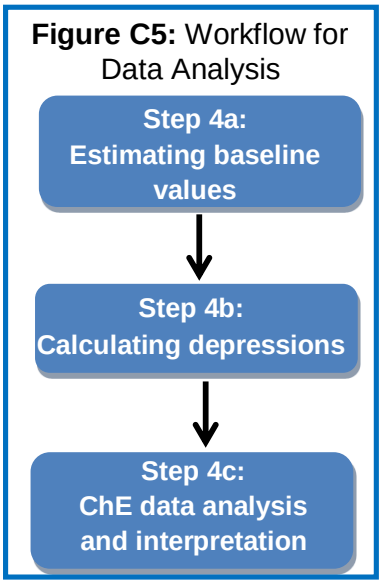


Figure C4: a) *Total number of ChE test results (RBC and Serum) before data clean-up (green), after additional data clean-up (red) and application of exclusion criteria (blue).* ***b)*** *Total number of individuals with ChE test results before data clean-up (green), after data clean-up (red) and application of exclusion criteria (blue).*

Figure C5: Workflow for Data Analysis



Step 4: Data Analysis

OEHHA analyzed the ChE data following the steps outlined in Figure C5.

Step 4a: Estimating baseline values

Since the purpose of the test for nearly all the records was not indicated or reliable, we explored alternative methods to analyze the data. We based our decision on the recommendations in the *Guidelines for Physicians,* which state that: 1) ideally, the baseline value should be the average of two or more tests taken

at least 72 hours but not more than 14 days apart following a 30-day exposure-free period[1] and 2) one baseline test is permissible if two were not obtained. Approximately half the population of presumed pesticide handlers appeared to have 14-day baselines. Their baseline values were calculated by averaging the two test results, and this method of baseline estimation was referred to as Approach 1. However, 14-day baseline estimates were not available for the rest of the population. In order to include these individuals in our analysis of depression frequencies, a different approach ("Approach 2") was adopted using the highest ChE test result obtained over the 2011-2013 period as an estimated baseline. Figure C6 illustrates how records from individuals with follow-up testing were divided into two groups to estimate the baseline.

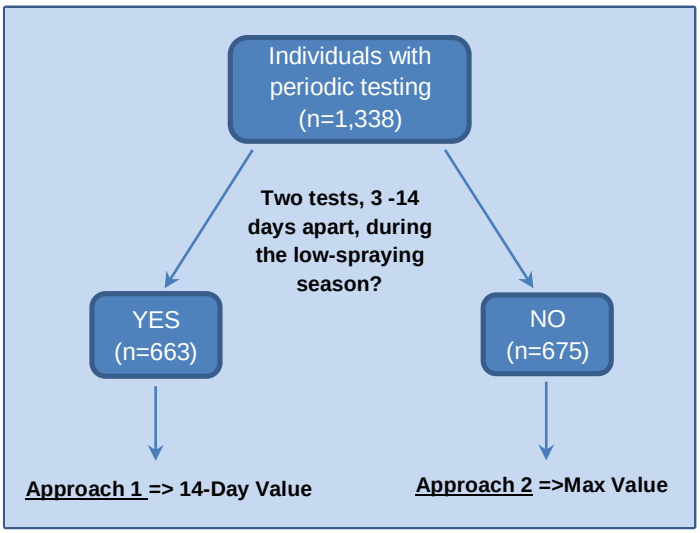


Figure C6: *Diagram of the two different approaches to determine baseline values for analysis.*

Approach 1. Baseline ChE activity level was determined by averaging results from two tests taken 3 to14 days apart during the low-spraying season[2] since pesticide handlers were most likely to be free of exposure during that period of the year. As recommended in the *Guidelines for Physicians*, if the first two baseline tests differed by more than 15% and a third test was performed within 14 days, the baseline was calculated as the average of the two closest results (Figure C7).

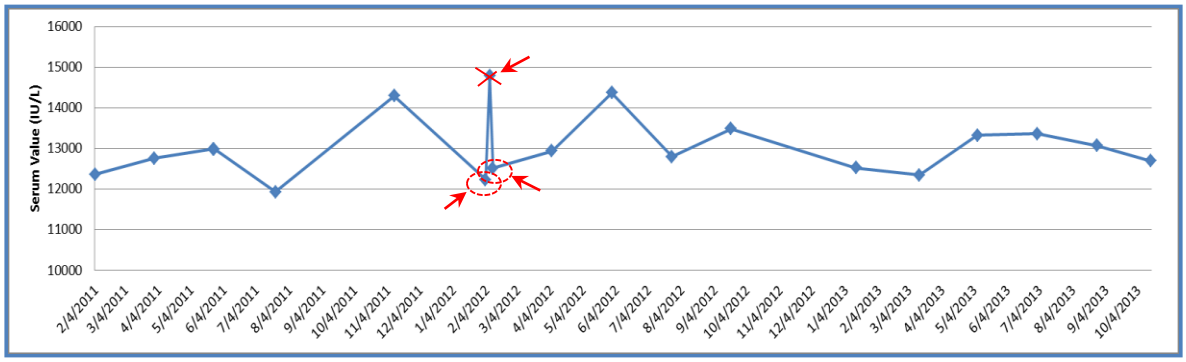


Figure C7: *ChE test results from an individual with three tests taken within 4 weeks. Since the three test results indicated by red arrows were taken over a short time period during the non-spraying season, we inferred that they were baseline test results. Furthermore, because the first two values differed by more than 15%, the baseline was estimated by averaging the first and third test result (i.e., the two circled data points).*

According to the *Guidelines for Physicians*, if a patient is recovering from ChE depression that required removal from OP/CB handling activities, the medical supervisor should promptly verify that ChE activities are returning to baseline. This situation also might lead to two samples being

[1] If two baseline tests differ by more than 15%, a third test should be performed, and the average of the two closest results should be used as an estimate of baseline ChE level.
[2] Five months with the lowest OP/CB pesticide use in California are November through March.

collected within a 14-day period. To avoid misidentifying "recovering" values as a baseline, we restricted the "baseline" period to the low-spraying season. Using statewide Pesticide Use Report data, we defined the low-spraying season as the five months with the lowest OP/CB pesticide use in California: November through March. Figure C8 illustrates how this decision rule was applied. On initial inspection, the figure appears to include three sets of paired baseline values. The two sets of two closely-spaced ChE test results surrounded by blue ovals probably represent the "true" baseline test results because they were taken during the non-spraying season, and they were used as such in our analysis. The red arrow indicates two closely-spaced ChE test results taken during the spraying season. These were probably not baseline measurements because they were collected during the spraying season and after the ChE activity level dropped below the first action threshold (<80% of baseline). In fact, they were likely to be taken during a recovery period following exposure to a ChE-inhibiting pesticide. The blue line represents the variation in ChE activity relative to the false baseline using the two values indicated by the red arrow. The red dotted line represents the variation in ChE activity relative to the baseline measurements surrounded by blue ovals.

Approximately half of the data (n=663) were amenable to this approach and they were analyzed using the 14-day baseline as the reference value.

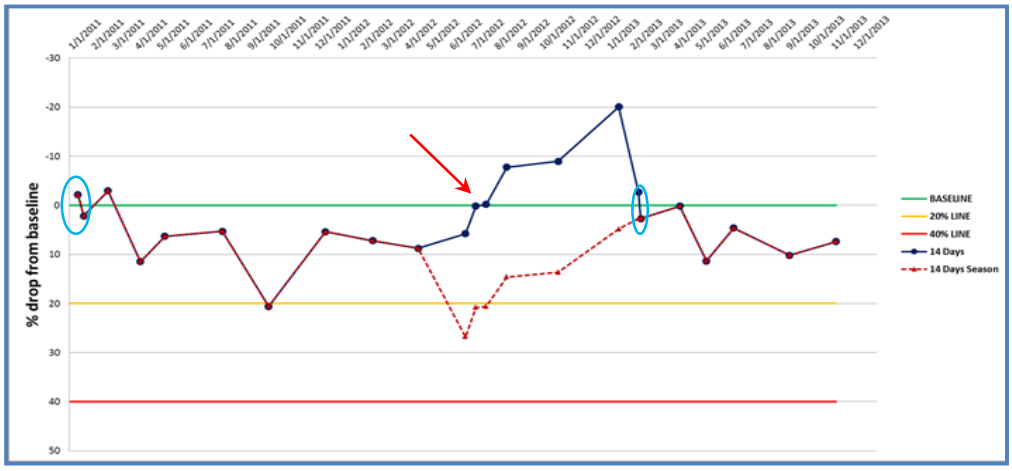


Figure C8: *Example of application of decision rules used to identify baseline estimates during non- or low-spraying season, and to reject samples collected within 14 days of one another during spraying season.*

Approach 2. For those data that were not amenable to Approach 1 (n=675), we assumed that the highest ChE test result obtained over the three-year period (2011-2013) was the baseline. We hypothesized that since baseline samples should be taken following a 30-day exposure-free period, the value of the baseline should be close or equal to the maximum ChE activity level observed.

In the main report, we compared frequency of depressions using Approach 1 on the population of individuals with a14-day baseline (n=663) to the frequency of depressions using Approach 2 on the entire population of individuals with periodic monitoring (n=1,338).

In this appendix, for the purpose of the discussion, the data set for subsequent analysis was comprised of records using ***either one or the other of the two approaches*** to define the baseline. Therefore if two successive sample results in an individual's chronological record did not appear to meet the first requirement (Approach 1), the alternative approach was used

(Approach 2). Since Approach 2 produced on average higher estimates of baseline activity than Approach 1, it led to a higher frequency of ChE depressions. Therefore the two approaches provided a range of estimates of the overall frequency and types of ChE depression. Use of both approaches also allowed us to include all suspected workers and doubled our sample size. To simplify the data analysis, all records were treated the same way once a baseline was determined. Results comparing both approaches are presented and discussed later in this Appendix.

We have compared frequency of individuals with depressions using Approach 2 on the total population of individuals (n=1,338) to the frequency of depressions obtained from the population of individuals without a 14-day value (n=675). As shown on Table C1, results from both populations are very similar.

Table C1: *Percentage of individuals with different levels of depressions using Approach 2 on all individuals (n=1,338) or just on individuals without a 14-day value (n=675).*

Action Level	RBC ChE		Plasma ChE	
	All Individuals	Individuals without 14-day values	All Individuals	Individuals without 14-day values
No action needed (80-100% of baseline)	87%	89%	62%	63%
Review of workplace practices (<80% of baseline)	9%	7%	33%	31%
Removal from further exposure (<60% of plasma baseline, or <70% of RBC baseline)	4%	4%	5%	6%

It is worth emphasizing that the need to use these two approaches to baseline estimation arose because the test purpose was seldom provided with the ChE test reports. Consequently, baseline ChE values were inferred solely from the data.

Step 4b: ChE data analysis and interpretation

We formulated five questions (A to E) to evaluate the Program and analyzed the ChE data to determine if it might provide insights and possible answers to these questions.

A. Can we infer from the reported ChE test results that workers who regularly handle category I and II OP and CB pesticides are participating in the Program?

Electronic reporting of ChE test results does not allow us to identify all the workers in California that handle OP/CB pesticides. It only provides a list of individuals who were tested for various reasons, and some of them might have been exposed to OPs/CBs. In an attempt to assess the degree of participation of workers in the Program, we analyzed the correlations between the temporal and spatial distribution of ChE test results and agricultural use of OP/CB pesticides in the state.

- **Geographic distribution of ChE test results and their association with pesticide use.**

We used geospatial analysis to determine if the overall number of ChE test results reported from each county was proportional to the amount of OP/CB used in that county. As shown in Figure C9, there is generally good correlation between geographic density of ChE test results and the areas of high pesticide use (Pearson's $r = 0.667$, $p < 0.0001$). In other words, the larger the quantity of OPs/CBs used in a county, the higher the number of ChE test results.

However, geographic analysis also revealed that there were very few ChE test results from several California counties that had relatively high OP/CB use (indicated with red arrow). Indeed, after applying the exclusion criteria, some counties with relatively high pesticide use (e.g., Butte, Glenn, Sutter, Yuba and Colusa counties in the northern Sacramento Valley) did not show any ChE test results. A lack of test results from these counties might be due to: 1) missing location information on the ChE test reports (16.1 % of total ChE test results), 2) uncertainty in identifying the employee's worksite (see explanations in the following paragraph), 3) seasonal migration of workers from one county to another, 4) small farms in these areas may have hired Pest Control Operators located in other counties to apply pesticides, and/or 5) employers failed to follow the Program requirements.

Geographic analysis also revealed that some counties with no or very low pesticides use (e.g., San Francisco) had disproportionally high number of tests. Further analysis revealed that these tests were from individuals not receiving periodic testing and most likely not participating in the Program (e.g., pre-operative testing, Alzheimer's drug monitoring, liver disease screening, and aging research studies).

Ideally, one would use employee's worksite data to generate the county-specific ChE test results and correlate the information with county-specific pesticide use data. However, employee's worksite data was not provided in the electronic ChE test reports. To overcome this data gap, we used the physician's location[3] to generate the county-specific ChE test results. This method may assign an employee to a wrong county if, for example, the employee was seen by a medical supervisor located in one county but was exposed in another county.

[3] When physician's location was missing, we used the location of the patient, the drawing lab or the employer instead.

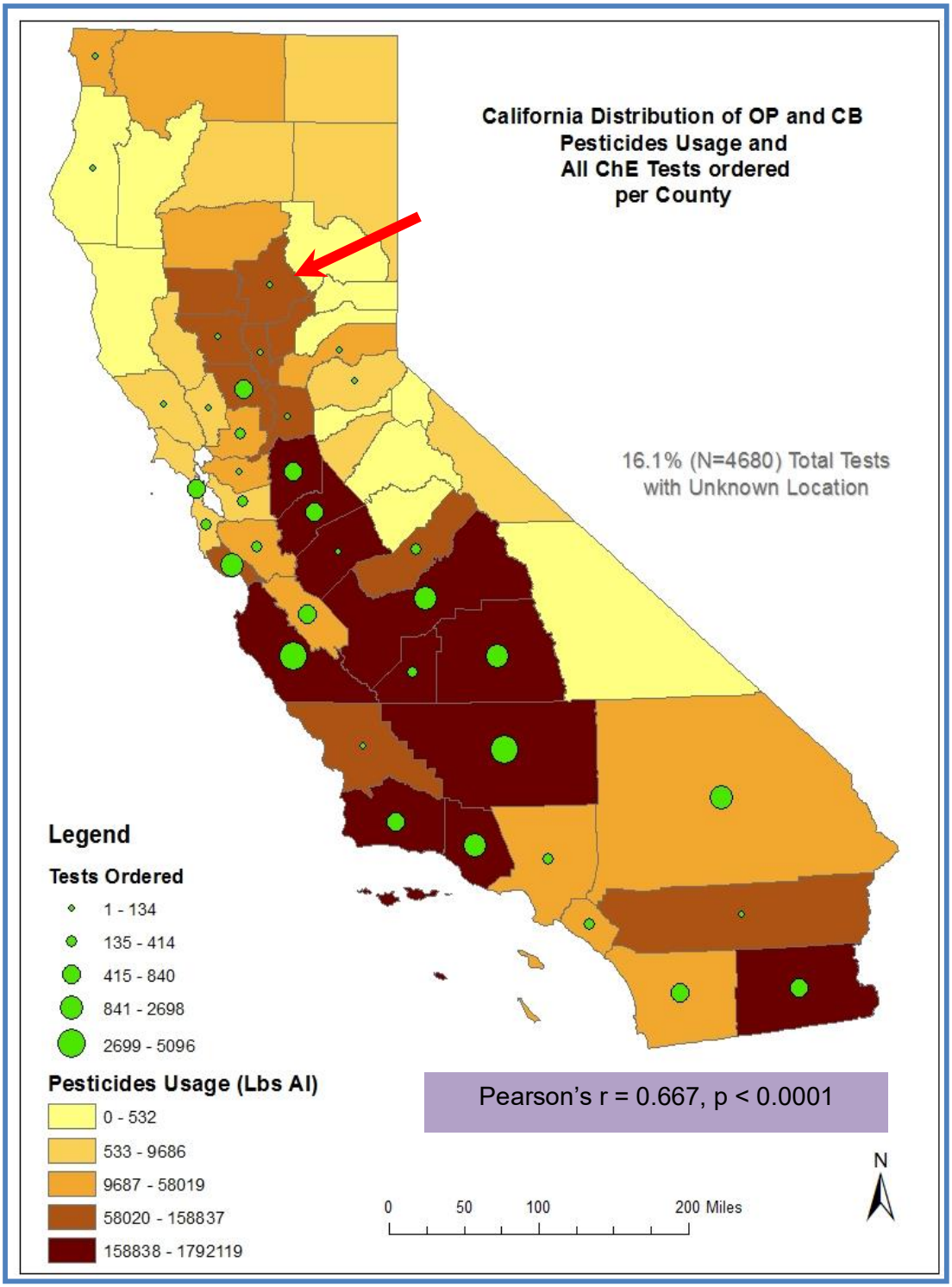


Figure C9: *Geographic distribution of OPs/CBs types I and II used (2011 – 2013) and number of ChE test results by county.*

- **Temporal distribution of tests ordered and their association with pesticide use.**

We used temporal analysis to determine if the monthly number of ChE test results reported was proportional to the monthly volume of OP/CB use. Figure C10 shows statewide monthly pesticides use with number of estimated baselines (a), and with number of estimated follow-up ChE tests (b) between 2011 and 2013 from dataset with periodic (follow-up) testing. As expected, the number of follow-up ChE tests (defined as total ChE tests minus baseline ChE

tests) showed a strong correlation with the volume of pesticide use (Pearson's r = 0.775, p < 0.0001) suggesting that an increase in the volume of OP/CB pesticide use leads to an increase in the number of follow-up tests being ordered (Figure C10b). Conversely, the number of estimated baseline ChE tests was inversely correlated (Pearson's r = -0.287, p < 0.1) with pesticide use (red line), reaching a peak between January and March of each year, just before the beginning of the spraying season (Figure C10a).

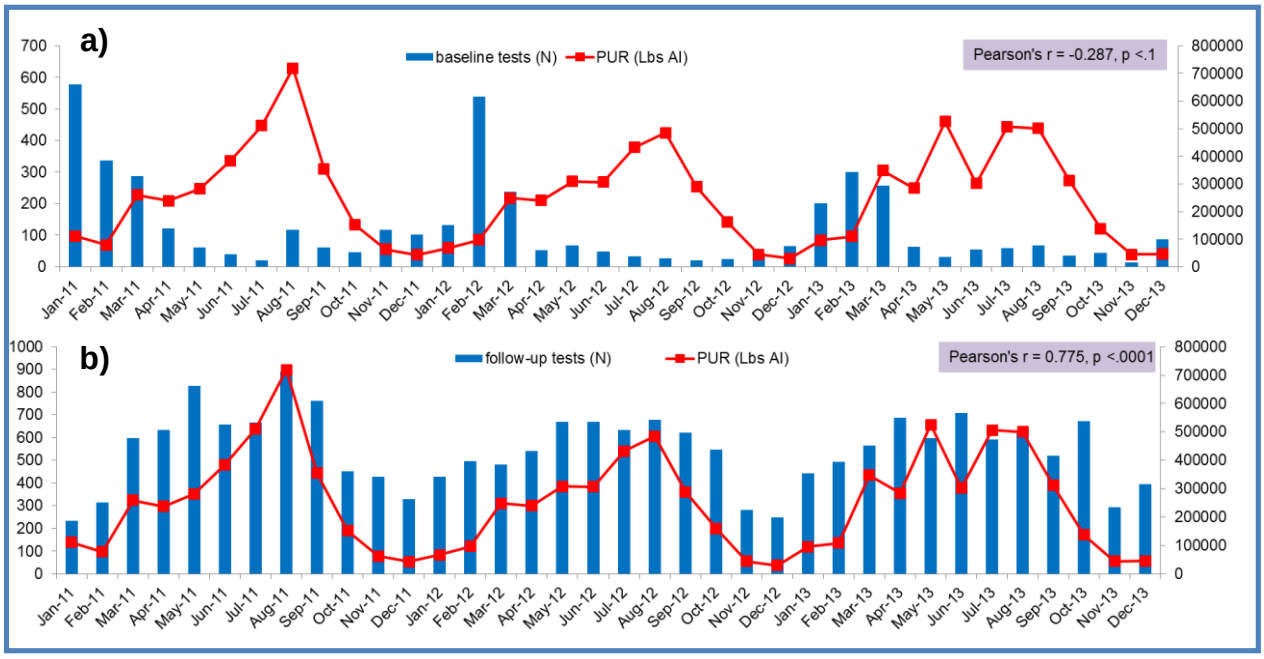


Figure C10: *Monthly OP/CB use (PUR) and* ***a)*** *number of estimated baseline ChE test results, and* ***b)*** *number of estimated follow-up ChE test results from dataset with periodic testing between 2011 and 2013. Red lines are pesticide use data (lbs AI/month, right y-axis) for all toxicity category I and II OPs and CBs. Bars are estimated number of monthly ChE test results.*

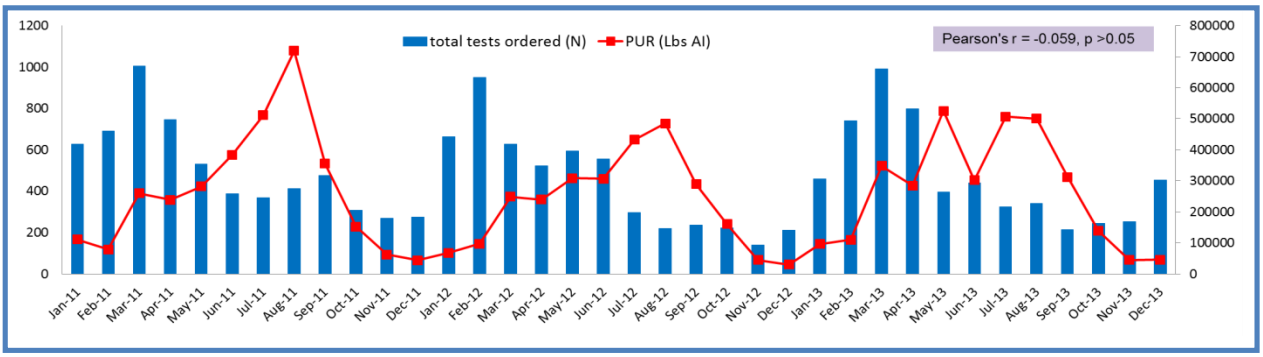


Figure C11: *Monthly OP/CB use (Pesticide Use Record) and number of ChE test results from dataset of individuals without periodic testing. Red lines are pesticide use data (lbs AI/month, right axis) for all toxicity category I and II OPs and CBs. Bars are estimated number of monthly ChE test results.*

Figure C11 shows statewide monthly pesticides use and number of tests ordered from the group of individuals that only had baselines taken and no other periodic testing (e.g., follow-ups). As expected, the number of tests from this dataset is similar to the one showing the baseline from the group with periodic testing (Figure C10a). Test results reached a peak between January and May of each year, just at the beginning of the spraying season (Figure C11). This suggests that a large number of these individuals participate in the Program even

though they did not have any follow-up testing. However some months with high pesticides use (e.g., June-August 2011) had significant number of tests. We presume that these test results are most likely from individuals not under the Program.

B. Can we infer from the reported ChE test results that depressions that exceed one or more of the action levels are occurring?

To investigate the frequency of ChE depressions (2011-2013), we used the dataset with routine periodic testing to look at the distribution of ChE test results that were 20, 30 or 40% below baseline (Figure C12). The proportion of ChE test results that appears to warrant action is relatively small. Three to twenty four percent of plasma ChE test results and 1-5% of RBC ChE test results appear to have required an evaluation of workplace practices, while only 1-5% of plasma ChE test results and <1-2% of RBC test results appear to have required removal of the worker from OP/CB handling activities. Nevertheless, from analysis of the ChE data alone, we cannot determine if any of these actions were actually taken.

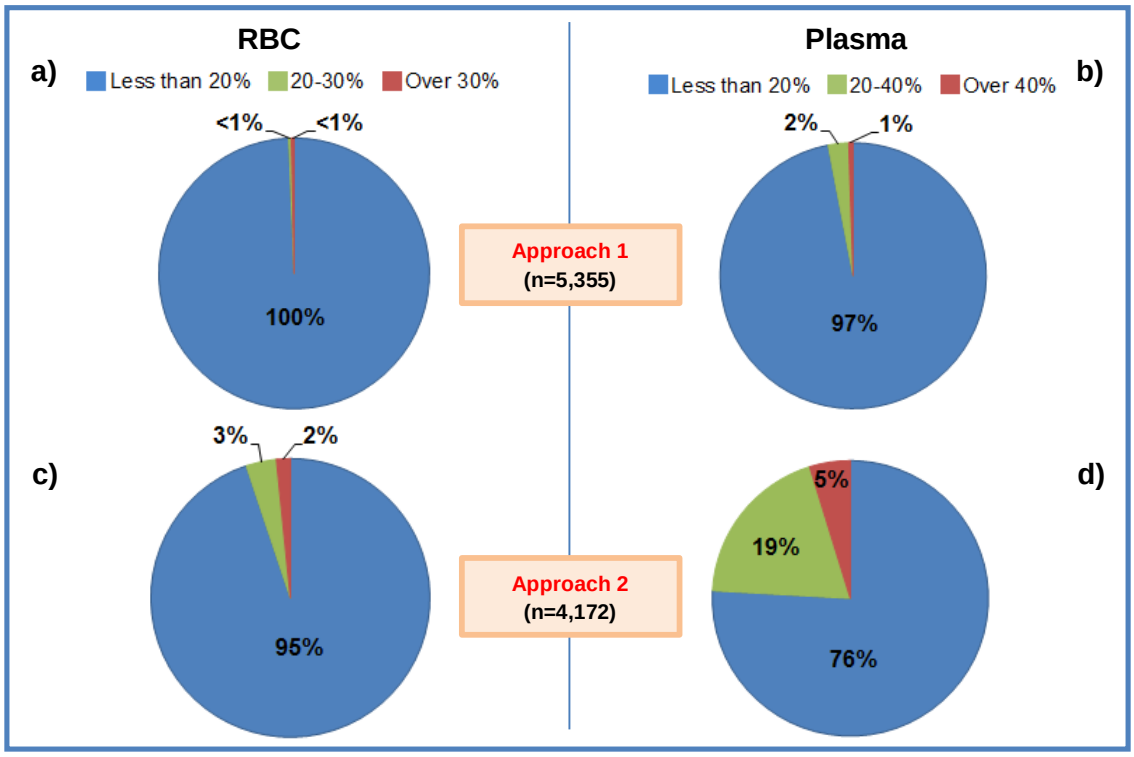


Figure C12: *Distribution of* ***test results from routine monitoring*** *with level of depressions requiring different level of action: no action needed (0-20%), review of workplace practices (20-30% for RBC and 20-40% for plasma), and removal from further handling of OP/CB (over 30% for RBC and over 40% for plasma) with Approach 1 (**a, b**) and Approach 2 (**c, d**).*

- **Geographic distribution of depressions and its association with the amount of pesticide use.**

We investigated the associations between the geographic distributions of apparent ChE depressions and county by county pesticide use to determine if depressions occurred more often in areas of high OP/CB use (Figure C13). The total number of depressions per county (represented on the map by the size of the circles) is significantly correlated with pesticide use

(Pearson's r = 0.315, p <0.05). The lack of ChE test results previously noted (Figure C9) in some counties with moderately high OP/CB use (e.g. northern Sacramento Valley), reduced the strength of correlation. In contrast, three high-use counties (Monterey, Ventura and Kern) had proportionally high number of depressions, and one county (San Benito) had a disproportionally large number of ChE depressions compared to the amount of OP/CB use.

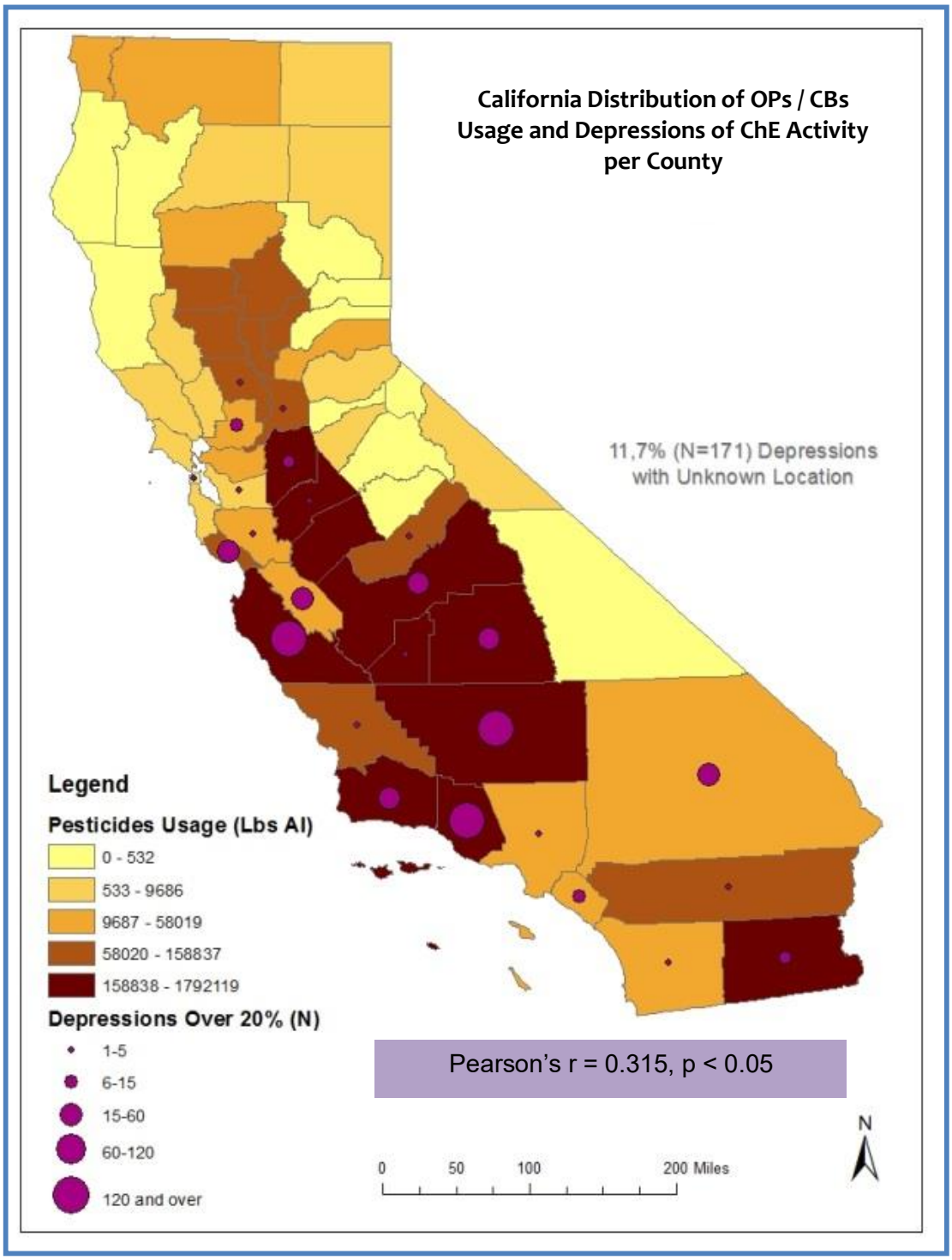


Figure C13: *Geographic distribution of OPs/CBs types I and II use and number of depressions by county across California (2011-2013).*

- **Temporal distribution of ChE depressions and its association with the amount of pesticide use.**

We investigated the associations between the temporal distributions of depressions and monthly pesticide use to determine whether depressions occurred more often during the months of high OP/CB use (Figure C14). Both monthly number (Pearson's r = 0.80, p < 0.0001) (Figure C14b) and monthly frequency (number of tests with significant depressions / total number of tests) (Pearson's r = 0.71, p < 0.0001) (Figure C14a) of depressions were strongly correlated with pesticide use.

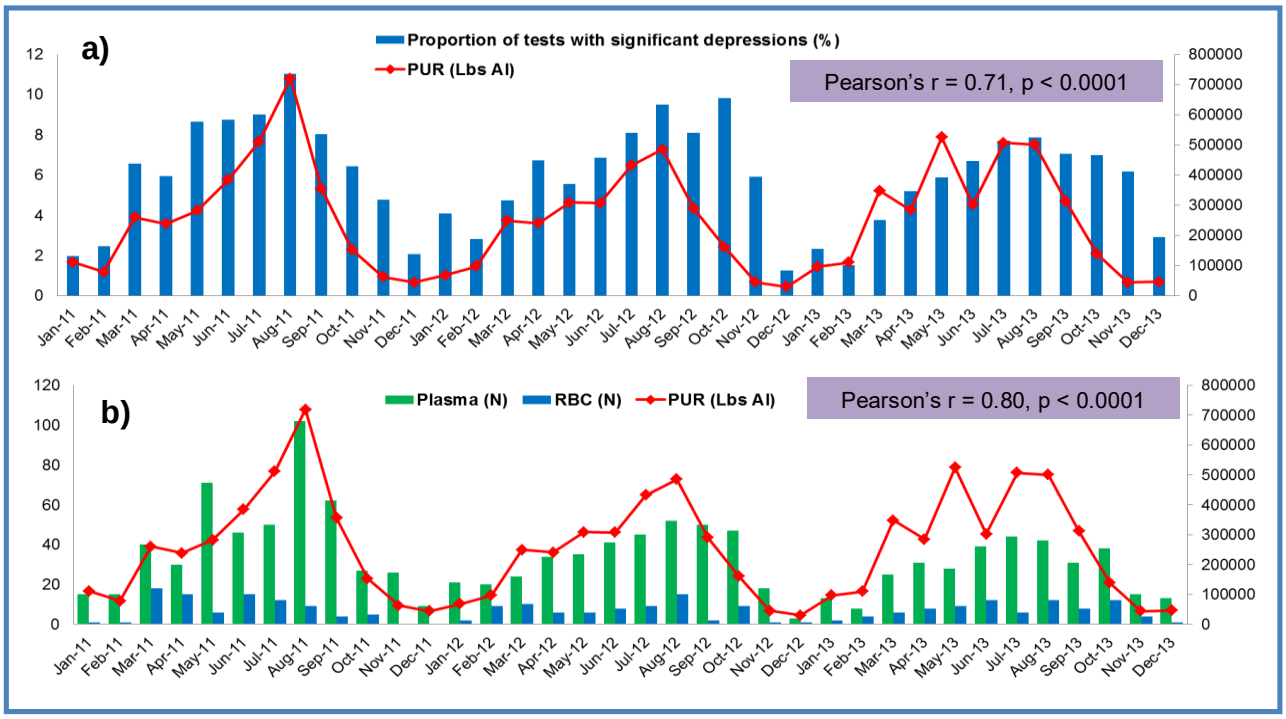


Figure C14: *Monthly pesticide use and ChE test results from 2011 to 2013. Red lines are pesticide use data (lbs AI/month, right axis) for all Toxicity I and II OPs and CBs.* ***a)*** *Bars are monthly percentage of ChE test results with depressions that met the minimum action level (>20%).* ***b)*** *Bars are number of Plasma ChE (green) and RBC (blue) depressions over 20%.*

C. Can we infer from the reported ChE test results that actions are being taken in the workplace in response to ChE testing?

There were 1,338 individuals who were tested numerous times over the three-year period, allowing a time course evaluation of ChE activity levels. Figure C15 represents five different patterns of individual ChE activity levels. These results illustrate variations in the frequency, magnitude and duration of ChE depression that meet or exceed the various action levels.

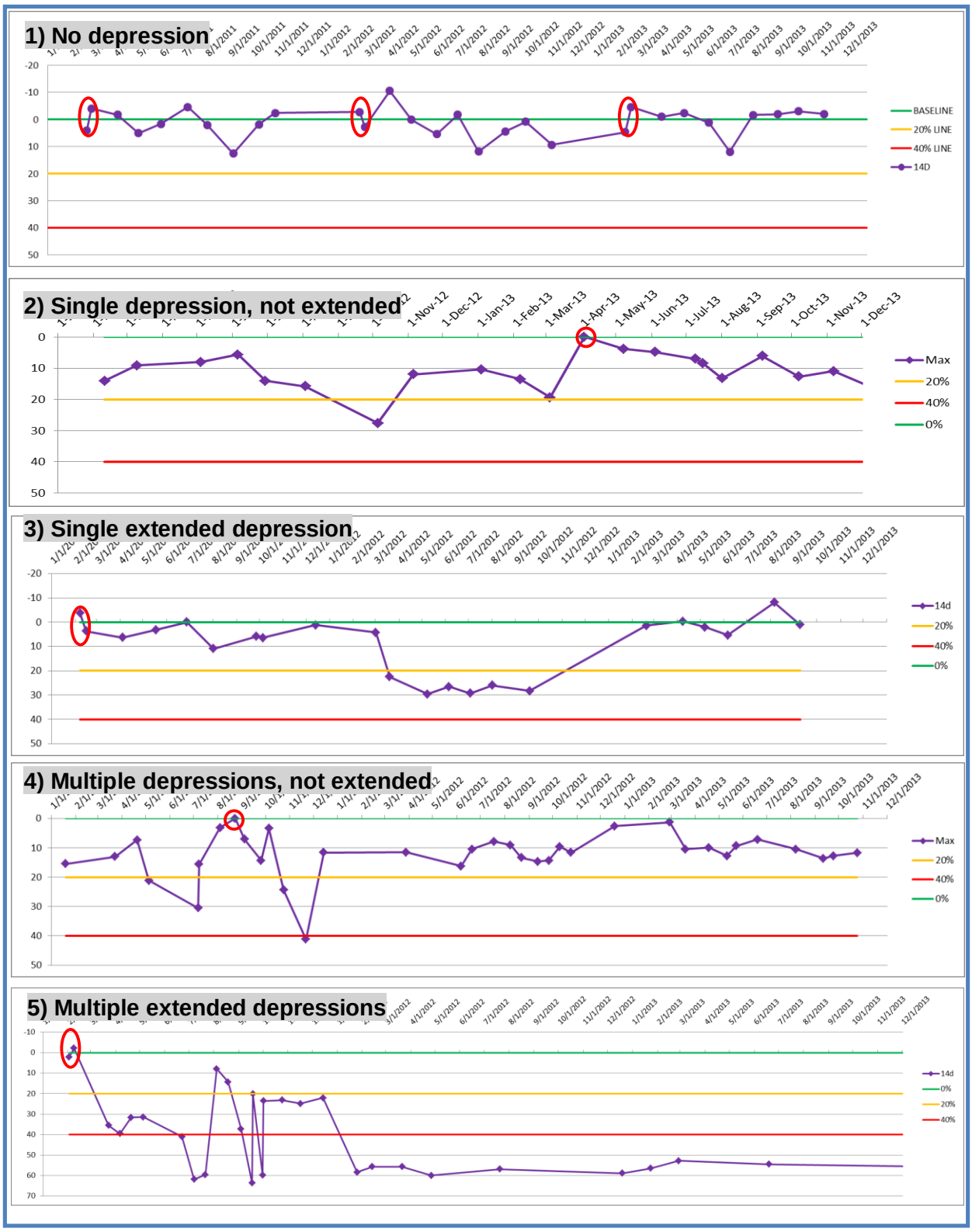


Figure 6: *Individual test results that represent different plasma ChE level patterns.* ***1)*** *no depression that exceeded action levels,* ***2****) single depression with prompt return to >80% of baseline level,* ***3)*** *single depression with slow return,* ***4)*** *multiple depressions with prompt return,* ***5)*** *multiple depressions with slow or no return. Y axis is percent depression from baseline. Green line represents the baseline of the individual. Red circled values are baselines.*

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A primary objective of the data analysis was to identify ChE test results that exceeded one or more action levels. For this purpose, we plotted the variation in ChE activity level of individual pesticide handlers over time. Often, the number of ChE tests over time is sufficient to provide some indication that a worker's activities were being managed in accordance with the recommendations of the *Guidelines for Physicians*, as reflected by their ChE test results. In some cases, insufficient records for individual workers prevented us from assessing whether corrective actions had been taken, or follow-up monitoring had been initiated, following ChE depression. Figures C16a and C16b are examples of longitudinal data with too few test results to indicate whether corrective action was taken (Figure C16a, which shows a 40% ChE depression with no subsequent test results), or to determine if a ChE depression was completely resolved (Figure C16b, which illustrates a 10-month gap between successive samples). Figure C16c is an example of time course data with sufficient test results to evaluate the pattern of ChE depression over the 3-year analysis period.

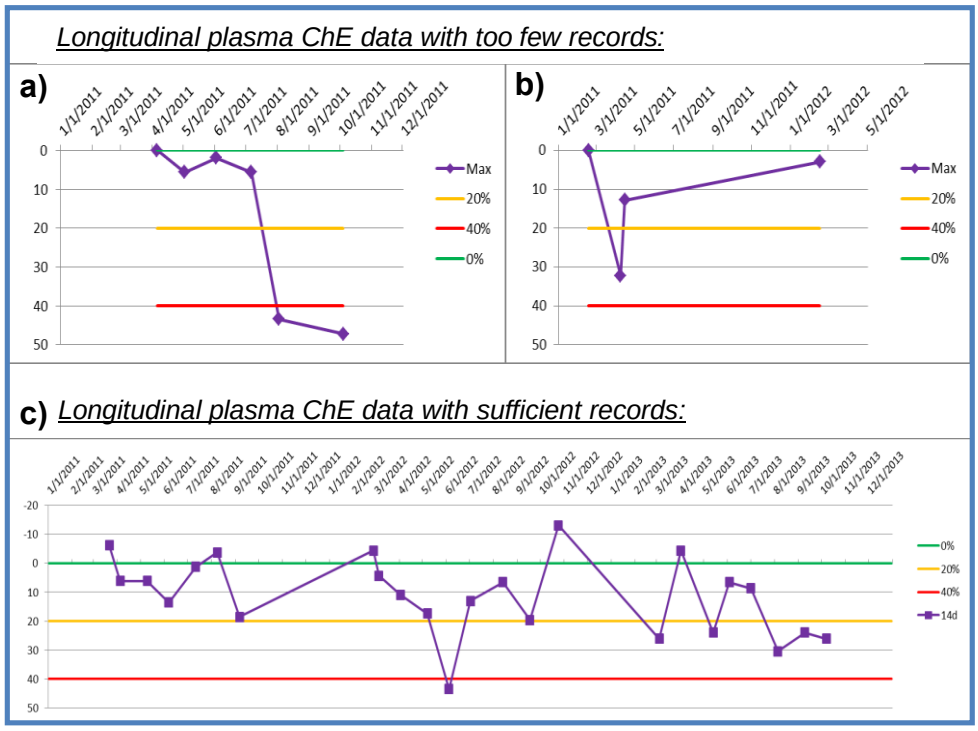


Figure C16: *Summary of visual examination of individual longitudinal variations extracted from the screening tool results. Examples show two individuals with too few records to interpret patterns of depression (**a** and **b**). Also shown is an example of an individual with sufficient records to identify ChE depression patterns (**c**). The Y axis is the percent depression from baseline.*

To examine if actions were being taken in the workplace in response to ChE test results, we investigated the number of individuals with ChE depression exceeding one or more action levels, the duration of time the ChE activity levels remained depressed (slow vs. rapid return to >80% of the baseline), and how often (single vs. multiple times) an individual experienced depressions of his/her ChE activity levels. For this purpose, we used SAS to develop a screening tool that allowed us to identify patterns of either RBC or plasma ChE variation over time.

Using the screening tool, we defined the five different time-courses of ChE activity over the 2011-2013 data analysis period (Figure C17):

1. **No** depression exceeding action levels: no depression below the minimum action level (<80% of baseline) occurred.
2. **Single** depression with **rapid** return to acceptable level: one or two consecutive depressions below the minimum action level occurred within a three month period, with rapid return to an acceptable level (>80% of baseline).
3. **Single** depression with **slow or no** return to acceptable level: three or more consecutive depressions below the minimum action level occurred within a three month period, with slow return or no return to an acceptable level.
4. **Multiple** depressions with **rapid** return to acceptable level: more than two discrete depressions below the minimum action level occurred, with rapid return to an acceptable level.
5. **Multiple** depressions with **slow or no** return to acceptable level: more than two discrete depressions below the minimum action level occurred, with at least one of these depressions returning slowly or not returning to an acceptable level.

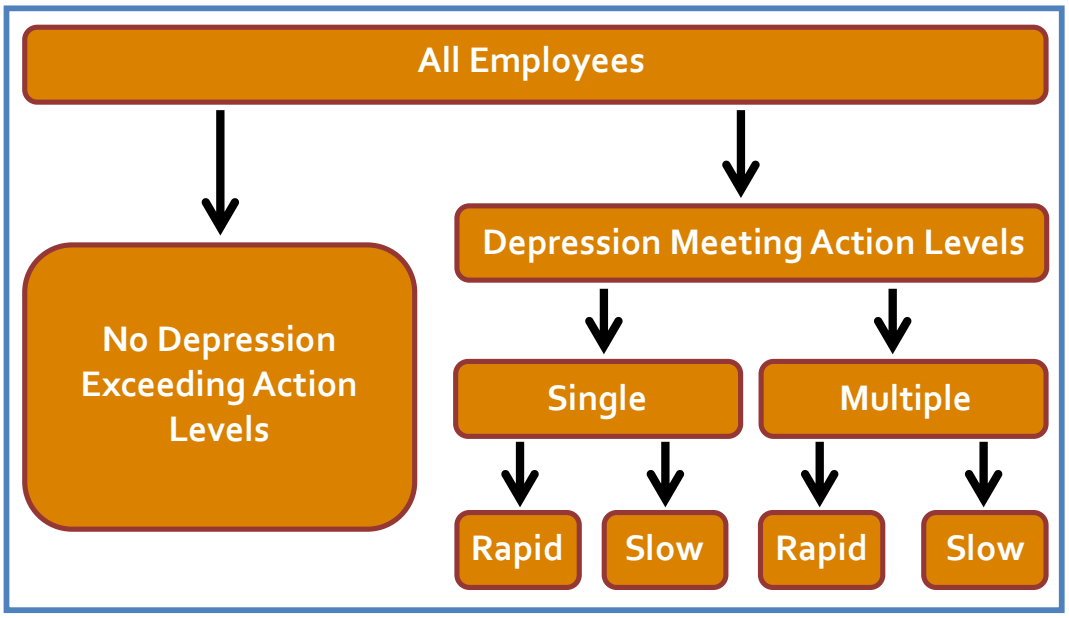


Figure C17: *Patterns of depressions of ChE activity*

We first investigated the number of individuals with ChE depression that exceeded any of the action levels, that is, those that required evaluation of workplace practices or immediate removal from work (Figure C18). Overall, 12-37 % individuals had at least one plasma ChE depression (> 20%) and 2-11% had at least one RBC ChE depression (>20%). However, only 1-6% of the individuals had at least one depression requiring removal from work based on plasma ChE depression (>40%) and only 1-4% of the individuals had at least one depression requiring removal from work based on RBC ChE depression (> 30%).

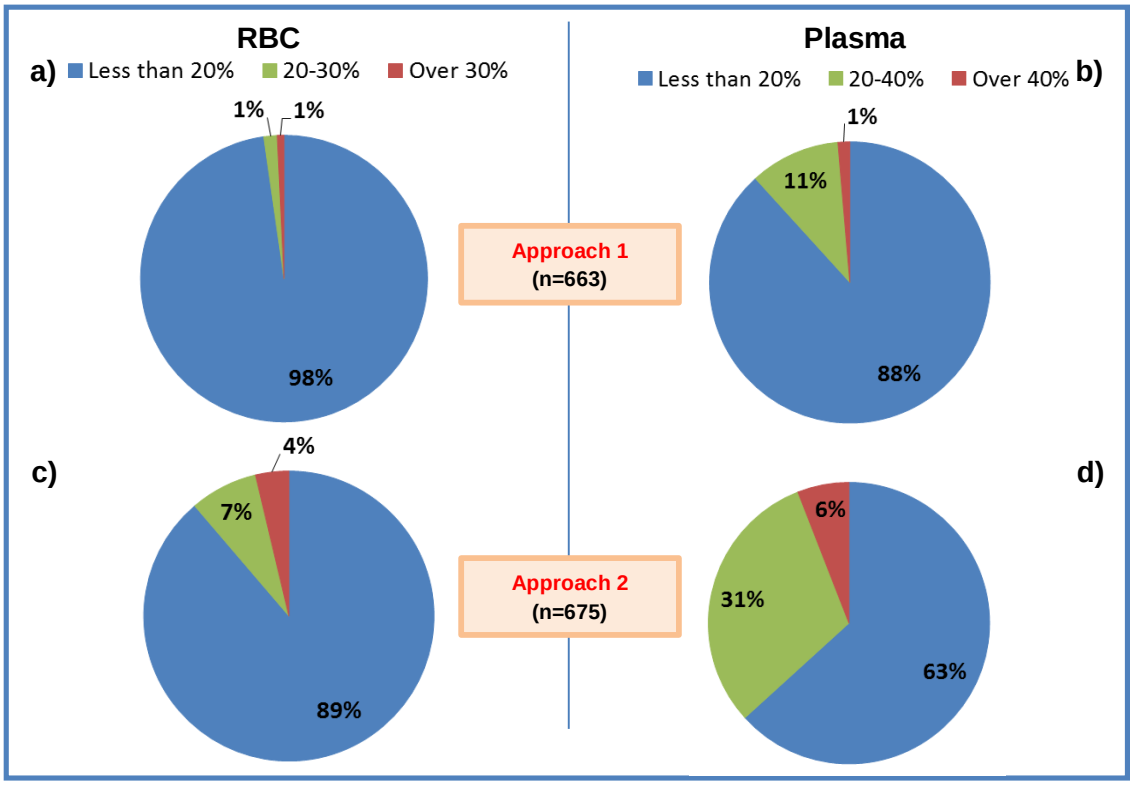


Figure C18: *Distribution of* ***individuals*** *with levels of ChE depression requiring different levels of action: no action needed (0-20%), review of workplace practices (20-40% for plasma ChE and 20-30% for RBC ChE) and removal (over 40% for plasma ChE and over 30% for RBC ChE) with* ***Approach 1*** *(**a, b**) and* ***Approach 2*** *(**c, d**).*

We used the screening tool to investigate the percentage of individuals who experienced repeated depressions of ChE and those whose ChE activity level remained depressed for an extended period of time. These results are shown in Figure C19. Sixty-three to eighty-eight percent of the individuals had no plasma ChE depression that exceeded an action level and 89-98% had no RBC depression. For individuals with plasma ChE depressions > 20%, 8-23% experienced multiple depressions and 4-14% had a single depression. With regard to RBC ChE activity levels, 1-5% of individuals had single depressions while 1-6% had multiple depressions. However, multiple depressions were generally short in duration and promptly returned to a level that would allow a worker to return to pesticide handling activities (i.e., >80% of the baseline). Two to eight percent of the individuals experienced multiple extended plasma ChE depressions while 1% or less experienced multiple extended RBC ChE depressions. These results suggest that in most cases, immediate action was taken following a depression of >20%, resulting in a prompt return to an acceptable ChE activity level. This analysis also suggests that, in some cases, long-term remedies may not have been implemented to prevent further excess pesticide exposure and consequent reoccurrence of ChE depression.

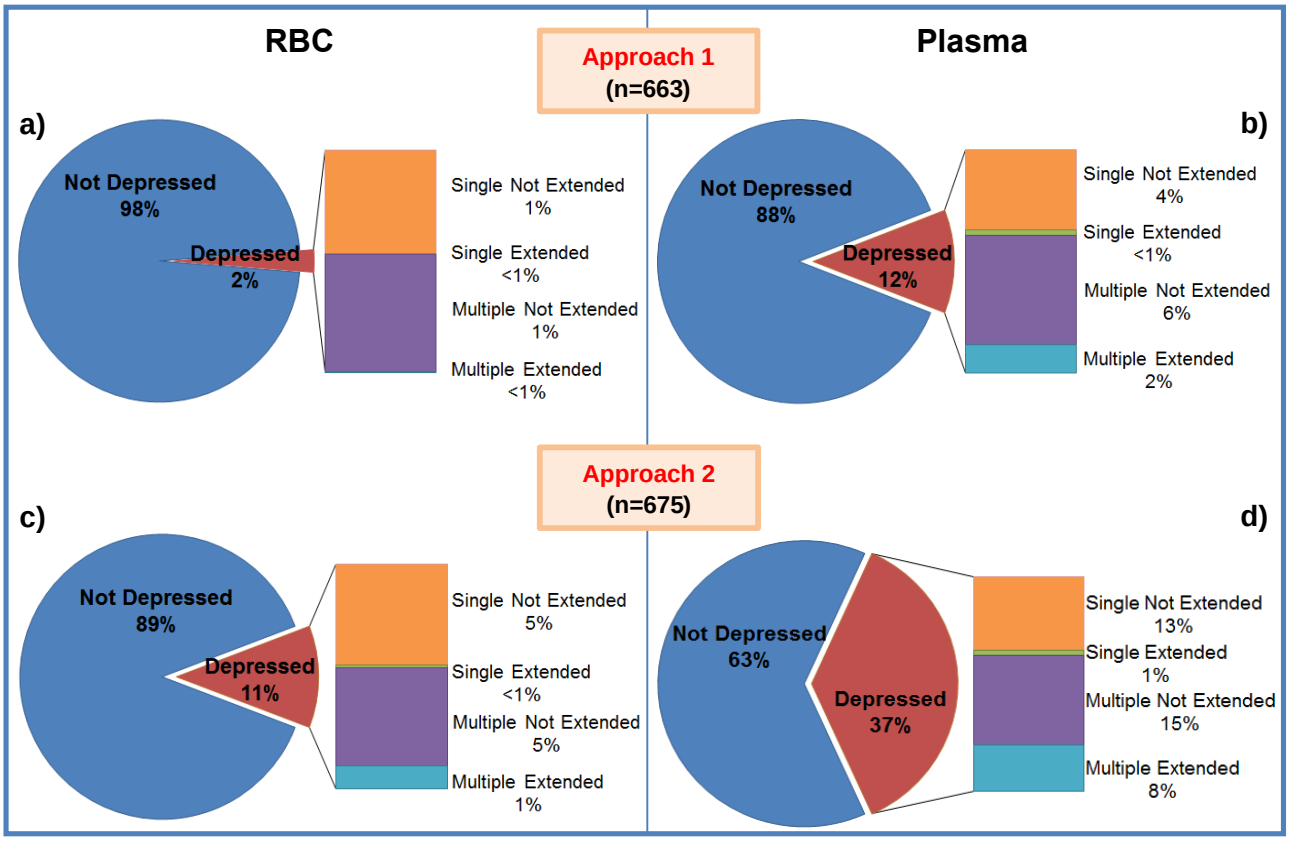


Figure C19: *Overall distribution of* ***individuals*** *by type of depressions (single, multiple, extended or not extended): RBC (left) and Plasma (right) with Approach 1 (**a, b**) and Approach 2 (**c, d**).*

- **Challenges resulting from not having the purpose of the test reported with the ChE data**

As mentioned earlier, it was not always possible to identify baseline test results in the dataset. To overcome this shortcoming, we used the two approaches described in Step 4a of this appendix ("Estimating baseline values"). However, both approaches are based on inferences and have limitations:

Limitations of Approach 1:

Reduce the sample size

Only approximately 50% of the ChE data were amenable to this approach (that is, had one or more 14-day baselines). The other 50% of the data had to be either evaluated using an alternative approach or discarded.

May potentially bias the findings:

It is possible that the individuals whose baselines were determined using Approach 1 were monitored more closely by both their employer, who was willing to cover the additional cost of a second baseline test, and their medical supervisor, who followed the *Guidelines for Physicians* recommendations more strictly. This may provide a biased picture on the overall effectiveness of the Program.

Error in defining the exposure-free period using the season:
Since we were unable to verify that an individual was exposure free for 30 days prior to collection of the first baseline sample, we limited the period for baseline samples to the statewide "low spraying" season. However, the spraying season varies within California. Some counties, especially those in southern California and along the central coast, do not have an "off-season" for agricultural production. This makes it very difficult to distinguish between baseline and post-exposure testing periods based solely on the traditional spring/summer/fall/winter seasons.

Limitations of Approach 2:

Overestimation of baseline value:
By definition, the baseline cannot be higher than the maximum ChE value. Therefore, using the maximum value as the baseline could lead to an over-estimation of the extent and frequency of ChE depressions. However, it provides a health-protective reference point for evaluating the blood ChE data when a 14-day baseline estimate cannot be determined.

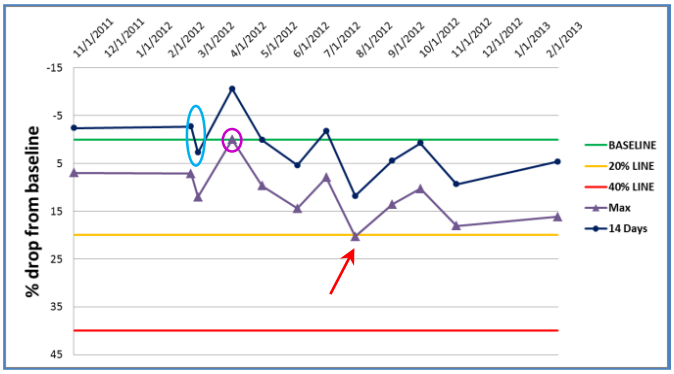


Figure C20: *An example of the error that might be introduced using Approach 2.*

An example of the error that might be introduced by Approach 2 is illustrated in Figure C20. The blue line represents the variations in ChE activity observed using the 14-day estimate of baseline (shown on the left side as the average of the two circled values). The purple line was obtained using the maximum value as the baseline (shown as the circled value from a sample collected in April, 2012). The red arrow represents the point where the 20% action level (yellow line) was exceeded using the maximum value baseline estimate but not the 14-day baseline estimate.

We estimated the degree of over-estimation of baseline activity introduced using Approach 2. The 14-day baseline estimate derived using Approach 1 was compared with the maximum value estimate derived using Approach 2 for those workers who had both values available. On average, the Approach 2 estimate of baseline was 12% higher than the estimate derived using Approach 1. Assuming that Approach 1 produces the "true" baseline (and there are uncertainties this regard, as noted above), Approach 2 may overestimate the number of depressions that exceed one or more of the action levels.

Earlier in this appendix, we presented results using Approach 1 for individuals who had 14-day baselines and Approach 2 for individuals who did not have 14-day baselines. We also compared results using each of the two approaches for individuals who had 14-day baselines (n=663) and obtained the following results:

1. Frequencies of *ChE test results* with depressions that met an action level (at least 20% below baseline) were much lower with Approach 1 than with Approach 2: <1 vs. 7 % for RBC ChE and 3 vs. 27 % for plasma ChE.

2. Frequencies of *individuals* with depressions that met an action level (at least 20% below baseline) were much lower using Approach 1 than Approach 2: 3 vs. 15 % for RBC ChE and 12 vs. 38 % for plasma ChE.

3. Regardless of which approach was used to establish a baseline ChE level, the relative proportions of single vs. multiple and extended vs. not-extended depressions were similar.

As expected, the evaluation using data generated by Approach 2 identified more depressions and more workers with at least one depression than Approach 1. But, as noted earlier, neither approach provides a definitive baseline; both approaches are based on inferences.

D. Does electronic reporting of ChE test results have an impact on the medical supervision program?

➢ Annual number of tests reported

In order to assess whether electronic laboratory reporting improved as a result of DPR's work with the analytical laboratories on their reporting practices, we evaluated the number of tests reported from 2011 to 2013. Figure C21 shows the number of test results before and after applying the exclusion criteria. The number of test results reported in 2012 and 2013 dropped by 40.5% compared to 2011, but the number of tests that we suspect were related to the Program declined by just 13.5%. This suggests that over the three year period, the laboratories improved their ability to eliminate irrelevant records from their reports. Therefore, DPR's efforts to improve the laboratory reporting process appeared to be effective and should be continued.

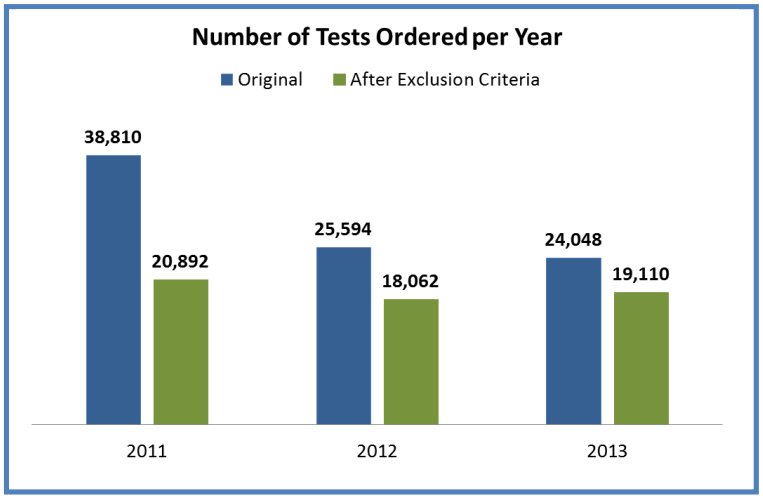


Figure C21: *Yearly number of tests before (blue) and after (green) applying all exclusion criteria*

- **Annual number of depressions**

Figure C22 shows the annual number of depressions observed, and the use of category I and II OP/CB pesticides from 2011 through 2013. There was a 30.4% decline in the number of depressions, but this decline did not coincide with a corresponding trend in OP/CB use. Improved work practices may have been responsible for the decline in depressions. Differences in the handling and/or processing of blood samples, or changes in the reporting process may also be contributing factors. Regardless of the cause, there was a general decline in ChE depressions over the three years.

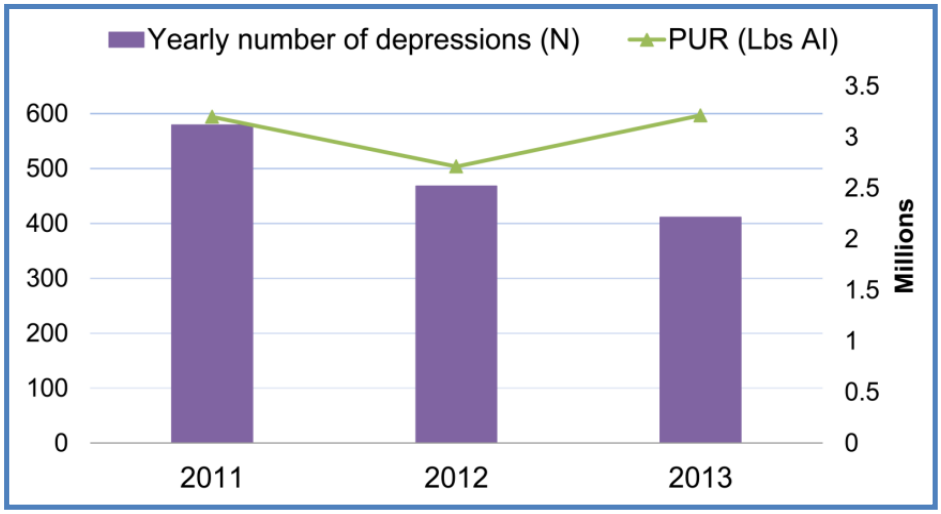


Figure C22: *Yearly number of depressions (purple bars, left axis) and yearly pesticide use (green line, right axis in millions of pounds AI, as reported in the PUR).*

E. Does intra- and inter-laboratory variability affect the reliability of monitoring of the workers?

- **Inconsistency of ChE test results reported from individual analytical laboratories**

Ninety-three percent of the Program-related test results were reported by three of the six laboratories [MEDTOX, Quest Diagnostics-Sacramento (QDI-SAC), and Quest Diagnostics-San Juan Capistrano (QDI-SJC)].

There was also a large difference in the frequency of ChE depressions detected by each laboratory. The percentage of depressions relative to the number of Program-related ChE tests (both RBC and plasma) reported by Physicians Automated Lab, Inc. (PALI) and MEDTOX were much higher than the other four labs (Figure C23). QDI-SJC had the overall highest number of depressions (n=562) from 2011-2013.

To explain the overall three-year decline in depressions (Figure C22) and the differences in the percentage of ChE depressions from the various laboratories (Figure C23), we analyzed the time course data from individual workers whose ChE records had been reported by each of the laboratories. We found that the high number of depressions observed with QDI-SJC appeared to be due primarily to frequent and large variations in ChE activity level that only occurred during 2011 (Figure C24). These cases of depression were the same as the ones we had previously identified from the geographic analysis in Ventura County. We are unable to determine the cause of this abrupt change in the variability of ChE test results but possible explanations may include improvements in pesticide handling practices or changes in blood sample handling procedures. Another possible explanation, based on information obtained from the focused growers' headquarters inspections, is that some workers continued to be tested even though they stopped handling OPs/CBs after 2011.

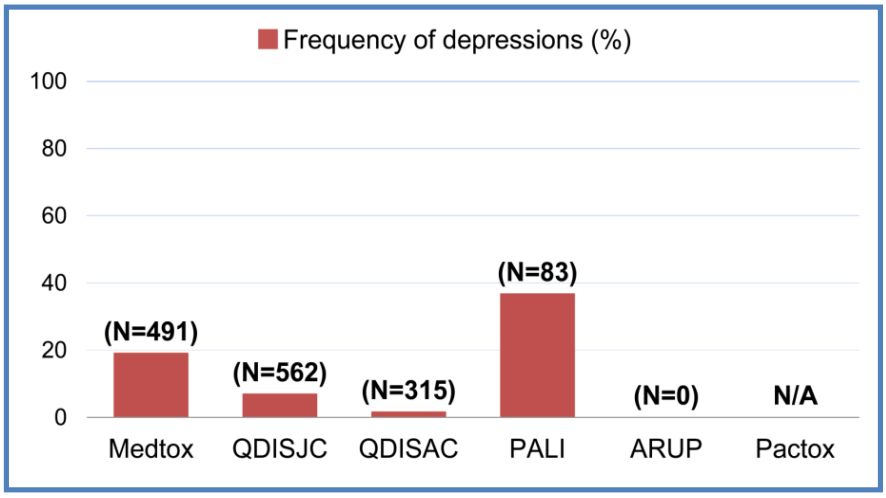


Figure C23: *Frequency of depressions (number of depressions divided by the total number of Program-related ChE test results), per laboratory. Three years of data were analyzed (2011-2013).*

Figure C24: *Individual longitudinal variations from max values of Plasma ChE from QDISJC. Y axis is percent depression from baseline.*

- **Inconsistencies in the "normal reference range" of blood ChE activity levels reported by the reference laboratories.**

While CCR Title 3, Section 6728 specifies that baseline and subsequent follow-up ChE assays should be conducted by the *same laboratory method*, the *Guidelines for Physicians* recommend using the *same laboratory* for baseline and follow-up testing. All six laboratories are approved by CDPH and use either the Ellman or Modified Ellman method for ChE analysis. Nevertheless, there is considerable variation in the normal ChE range that the six laboratories provided to us (Table C2) clearly indicating that it is important to follow the *Guidelines for Physicians* recommendation. Of the ChE test results from the 1,338 suspected workers (2011-2013), 91% of the blood samples were analyzed by the same reference laboratories. Eight percent of the samples were analyzed by two different laboratories during the 3 year period, but at each spraying season both baseline and follow-up tests were analyzed by the same laboratory. Only 1% of the tests results were analyzed by different laboratories over a spraying season Figure C25).

Table C2: *Normal Reference ranges for ChE test results (IU*

Laboratory	RBC		Plasma	
	Low	High	Low	High
Pactox	6.6	15.5	1.8	5.2
Pali	11.19	16.7	3.17	6.33
ARUP	7.9	17.1	2.9	7.1
Medtox	6.3	13	1.9	5.5
QDISAC	9.57	15.03	2.5	7.03
QDISJC (women)	9.57	15.03	2.5	6.2
QDISJC (men)	9.57	15.03	3.33	7.03

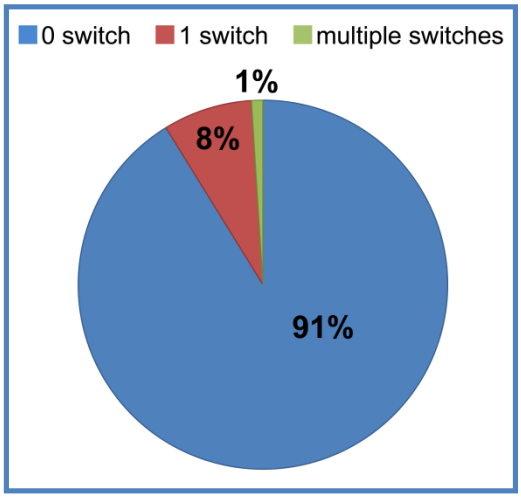


Figure C25: *Percentage of individuals whose blood specimens were sent to one, two or multiple labs for analysis over the 3 years.*

If blood samples from a single individual were analyzed by different reference laboratories, it would be difficult to interpret the results over time since changes in the ChE activity level may reflect inter-laboratory variation, not exposure to OPs/CBs. For this reason, all blood samples from an individual should be analyzed for ChE by the same reference laboratory.

Summary of Findings from Analysis of Electronically-Reported ChE Data

Laboratory-based reporting is a valuable tool for evaluating the Program. ChE test reports can be used to evaluate the implementation of the Program and assess its effectiveness on a statewide basis.

Analysis of electronically-reported ChE data allowed us to draw the following conclusions:

1. The number of workers who participate in the Program was proportional to OP/CB pesticide use.
   - ❖ The temporal distribution of the *number of estimated baselines* was inversely correlated with pesticide use. Conversely, the number of estimated follow-up tests and the number of ChE depressions were directly correlated with pesticide use.
   - ❖ When the data were analyzed on a county-by-county basis, there was good concordance between the geographic density of the *number of ChE test results* and the relative amount of OP/CB pesticide use, although some exceptions were also observed (for example, counties in the northern Sacramento valley). This suggests that in areas with heavy pesticide use, there is a high degree of worker participation in the Program.
   - ❖ Similarly, there was a good concordance between the geographic density (on a county-wide basis) of the *number of ChE depressions* and the relative amount of OP/CB pesticide use.
2. There were large differences in the frequency and magnitude of depressions using the two approaches used to identify baseline ChE activity levels. Regardless of the approach used, the relative proportions of single, multiple, short-term or extended depressions were similar.
   - ❖ Most of the workers did not have a ChE depression that reached a level requiring any action to be taken by the medical supervisor or the employer.
   - ❖ Some cases of ChE depression reached a level requiring an assessment of workplace practices. Even fewer cases required immediate removal from work.
   - ❖ There were also cases where 1) ChE activity levels remained depressed for an extended period of time (several months) and 2) ChE activity levels were depressed repeatedly.
   - ❖ Workers who experienced depression of their plasma ChE activity level had repeated depressions more often than single depressions. Most of these depressions were followed by a rapid return to an acceptable ChE activity level. This suggests that, in most cases, prompt actions were taken based on the recommendation from the medical supervisor, but long-term remedies were not implemented to prevent subsequent OP/CB exposure.

Our analysis of ChE test results and laboratory-based reporting also helped us identify program elements that can be improved. For example, the distribution of ChE test results that exceeded action levels could be interpreted as an indicator of the effectiveness of the Program. Ideally, we would hope to see minimal number of cases of ChE depression, or if there is a single ChE depression, the level does not exceed 30% below RBC ChE baseline or 40% below plasma

ChE baseline. This would indicate that the employer took action to prevent additional exposure. These patterns of depression and recovery could be identified from our analysis of the ChE test results.

However, analysis of ChE data was hampered because critical information was not provided in the submitted test reports. We encountered numerous obstacles in effectively analyzing the ChE test results, primarily due to not having the purpose of the ChE test indicated in the reports. Lacking the information on the purpose, we have to use certain assumptions in evaluating the ChE data, and that could affect our findings. In addition, the large number of extraneous ChE test results (not related to the Program) compromised our ability to focus our analysis on the population of interest (i.e., OP/CB pesticide handlers). As a result, we applied broad inclusion criteria to increase our confidence that the data reflected the work activities of all workers in the Program. Limiting analysis of ChE test results to agricultural workers will greatly improve the ability of DPR and OEHHA to use these test results to evaluate the medical supervision program. Better quality data would not only improve our ability to evaluate the Program and make recommendations for improvement but also help us meet our mandates to protect California's agricultural workers.

Appendix D: MEDICAL SUPERVISOR SURVEY

A mail-in medical supervisor survey was conducted to supplement the ChE test results analysis. The goals of the survey were to:

- Confirm that persons identified as ordering physicians in the submitted ChE test results are medical supervisors.
- Evaluate a medical supervisors' familiarity with the reporting requirements of HSC §105206.
- Evaluate a medical supervisors' understanding of his or her role and responsibilities as a medical supervisor (HSC §105206, 3CCR §6728, OEHHA's *Guidelines for Physicians*) as well as compliance with specific elements of the Program (3CCR §6728).

There were 1,021 names recorded as an 'ordering physician' on the submitted ChE test reports from 2011 to 2013. We used *BreEZe*[1] and/or an extensive internet search to confirm that an 'ordering physician' was a California-licensed physician. Of the possible 1,021 names, we uncovered a variety of occupations of the persons who ordered a ChE test. Confirmed physicians practice various specialties ranging from Occupational Medicine to Psychiatry. Non-physicians, such as nurses, physician assistants, front office administrators, and farm managers, were also entered as the 'ordering physician'. The professions of individuals identified as an 'ordering physician' are summarized in Table D1.

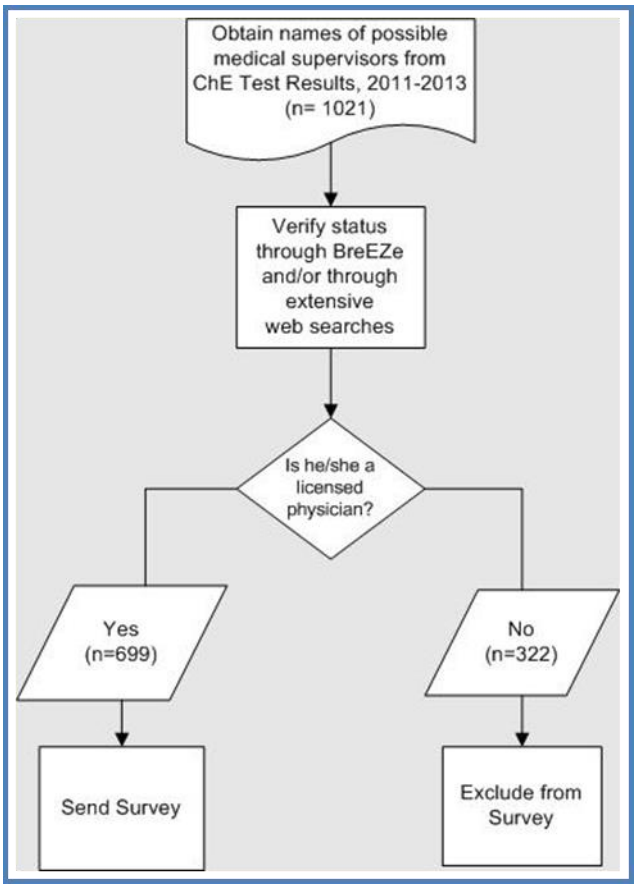


***Figure D1**: Flowchart to identify recipients of the Medical Supervisor Survey.*

Individuals that we could not confirm were licensed physicians were excluded from receiving the survey (Figure D1). We were aware that this would exclude healthcare providers who could potentially be working under a medical supervisor. However, we wanted to focus on the licensed physicians because the Program specifies that an employer enters a contract/agreement with a physician for medical supervision services. A total of 699 licensed physicians were mailed a survey.

[1] *BreEZe* is the Department of Consumer Affairs' web-based licensing and enforcement system which allows license searches (https://www.dca.ca.gov/webapps/breeze/about_breeze.php).

Results of the Survey

Of the 699 surveys sent to physicians, 257 (37%) were returned completed and 41 (6%) were returned as 'undeliverable'. Only 31 (12%) of the 257 mailed-in responses confirmed that the respondent was a medical supervisor from 2011 to 2014. (Table D2)

We attempted to call the 401 (57%) physicians who did not return the questionnaire to complete the survey over the phone or to offer resending the survey. On some of our calls – using telephone numbers obtained through internet searches – we were informed that the number called was for a hospital or medical center. These facilities informed us that the physician was not listed in the hospital directory, no longer working at that facility, or had retired. On other calls, we were placed on hold for periods exceeding 15 minutes and we had to end the call.

Reason for Exclusion	Count
1. Not a Medical Doctor (MD/DO)	
a. Certified Nurse Midwife	1
b. Chiropractor	2
c. Naturopathic Doctor	1
d. Nurse Practitioner	35
e. PhD	1
f. Physician Assistant	52
g. Registered Nurse	7
2. Deceased	1
3. No license found in BreEZe	9
4. Occupational Health physician for Non-Agriculture employees1	2
5. Physician, license could not be verified	11
6. Unknown	200

Table D1: *Professions of individuals who were excluded from the Medical Supervision Survey.*

Table D2: Response to DPR's Medical Supervisor Survey		
Number of physicians who were mailed a survey		699
SURVEY OUTCOME		
Survey returned as undeliverable		41
Survey completed and returned		257
a. Respondent confirmed that they were NOT a medical supervisor	226	
b. Respondent confirmed that they were a medical supervisor	31	
Follow-up to physicians who did not return survey and survey was not returned undeliverable		401
a. Respondent confirmed that they were NOT a medical supervisor	41	
b. Respondent confirmed that they were a medical supervisor	10	
c. Called and survey resent – but no response	59	
d. Called but no response	138	
e. Not contacted	153	

As of December 2014, we made 248 (62%) calls. However, only 51 calls were successful with another 10 physicians confirming that they were a medical supervisor. For the remaining 197 calls, we were referred to a medical assistant or an office manager who requested that the survey be resent to them (Table 9). To date, and even after several follow-up attempts, we have yet to receive the surveys from these physicians. Of the 153 physicians that have not been contacted, 57 (38%) were from predominantly urban counties (Los Angeles, San Diego, Santa Clara). Moreover, the top three specialties of the physicians in these counties were Internal Medicine, Family Medicine and Anesthesiology suggesting that they are not involved in the Program.

A. Confirmed Medical Supervisors

Thirty seven of the 41 confirmed medical supervisors reported that they were acting in that capacity when we conducted the survey in 2014. Four said that they were medical supervisors only from 2011 to 2013. The 41 medical supervisors we confirmed through the survey is much less than the 101 medical supervisors identified by OEHHA through their survey in 1995 (*Ames and Menendez, 2001*). A possible explanation for this difference is the 73% decrease in the use of all ChE-inhibiting pesticides over the past 20 years (Figure D2) which may have resulted in the need for fewer medical supervisors.

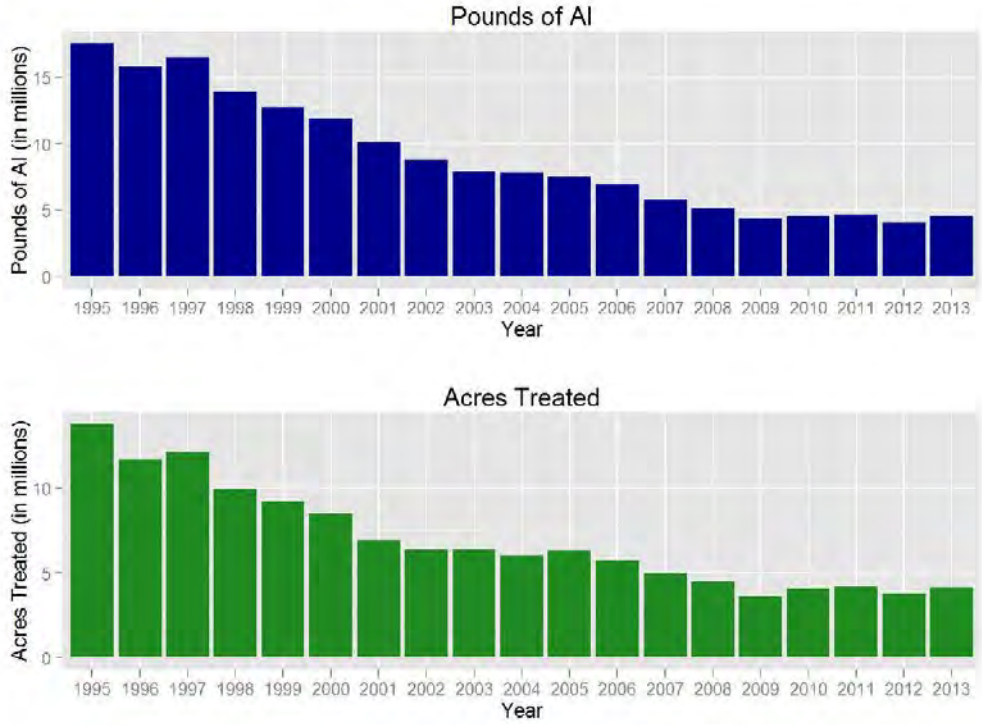


Figure D2: *Use trends of ChE-inhibiting pesticides. These pesticides are organophosphate and carbamate active ingredients. Reported pounds of active ingredient (AI) applied include both agricultural and non-agricultural applications. The reported cumulative acres treated include primarily agricultural applications. Data are from the Department of Pesticide Regulation's Pesticide Use Reports. Source: Summary of Pesticide Use Report Data - 2013. Accessed from http://www.cdpr.ca.gov/docs/pur/pur13rep/figures/fig7.htm on July 10, 2015.*

B. Region and Specialty (Figure D3)

- Over half of the confirmed medical supervisors were located in Central California (51%, n=21). The geographic distribution of medical supervisors in the survey is consistent with DPR's PUR database which shows that growers who apply OP/CBs pesticides were mostly in the state's central region (Figure 2).
- The majority of the medical supervisors who responded specialize in occupational medicine (71%, n=29). This branch of clinical medicine centers on preventive medicine and management of illness, injury or disability that is related to the workplace. The remaining physicians specialize in family medicine (20%, n=8), internal medicine (2%, n=1), or other unspecified medical specialty (2%, n=1). Two medical supervisors (5%) did not indicate their specialty.

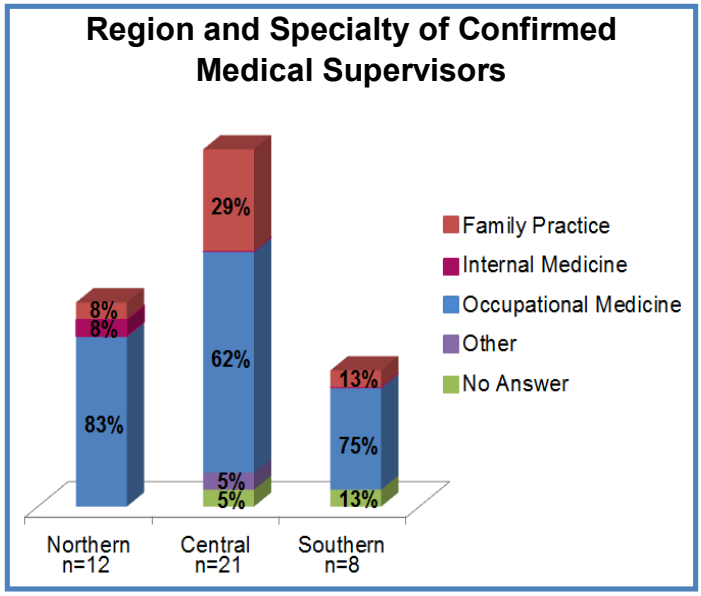


Figure D3: *Region and specialty of confirmed medical supervisors. (Total number of medical supervisors who responded to the survey, n=41.)*

C. Medical supervisors contract with employers

- Thirty-four of the 41 confirmed medical supervisors listed a total of 105 employers with whom they were contracted. The remaining seven medical supervisors did not write down the name of a grower/employer with whom they had a contract. Nine of the 105 employers were identified as a client by more than one medical supervisor.
  - ❖ Fifteen (44%) medical supervisors reported having a contract with only one employer. Nineteen (56%) medical supervisors reported having a contract with more than one employer (range: 2 - 27) with two stating that they had a contract with more than 10 employers.

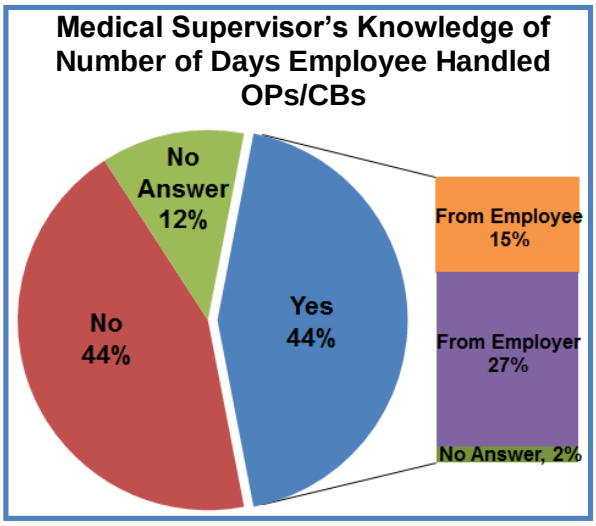


Figure D4: *Information on the number of days an employee handled OPs/CBs and who provided it to the medical supervisor. (Total number of medical supervisors who responded to the survey, n=41.)*

D. Medical supervisors' activities

➢ Knowledge of patient's OP/CBs exposure (Figure D4)

The Program requires employers to provide medical supervision for any worker who regularly handles OPs/CBs (more than six days in a 30-day period).

- Eighteen (44%) medical supervisors indicated they were aware of the number of days an employee handled OP/CBs within a 30-day period. Two-thirds stated that this information was provided by the employer (n=11) and a third were informed by the employee (n=6).

➢ Obtaining ChE levels for employees (Figure D5)

The Program requires that medical supervisors establish baseline ChE levels that shall be verified every two years. Routine monitoring shall be at intervals specified in writing by the medical supervisor, or every 60 days if the medical supervisor has made no written recommendation for continued periodic monitoring.

- *Baseline ChE levels*: The majority of medical supervisors obtained baseline ChE levels for new hires (73%, n=30) while only four (10%) did not. Seven (17%) medical supervisors did not respond to this question.
- *Frequency of obtaining baseline ChE levels*: Twenty-seven (66%) medical supervisors obtained baseline ChE levels every 2 years while 6 (15%) did not. Eight (20%) medical supervisors did not respond.
- *Routine monitoring/ Frequency of periodic testing*: Twenty two (54%) medical supervisors conducted periodic monitoring of employees while 11 (27%) did not. Eight medical (20%) supervisors did not respond. Of those who performed periodic monitoring, 17 (77%) conducted ChE testing every 60-days, 3 (14%) every 30 days, and 2 (9%) every 365 days.

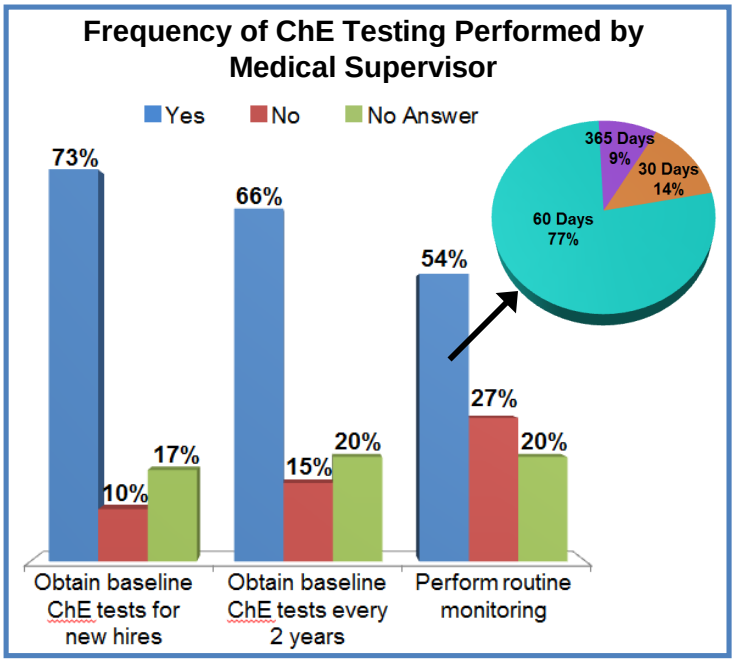


Figure D5: *Frequency medical supervisors obtain baseline for new hires, verifying baselines and perform periodic monitoring. (Total number of medical supervisors who responded to the survey, n=41.)*

➢ **Informing a worker of his/her ChE test results and recommendations from the medical supervisor (Figure D6 and Table D3)**

HSC §105206 requires that medical supervisors, within 14 days of receiving the ChE test results, shall ensure that the person tested receives a copy of the results and any of their recommendations. However, neither HSC §105206 nor the Program specifies the method in which employees receive their test results (from the medical supervisor or via employer).

- Nineteen (46%) medical supervisors informed both the employee and employer of the ChE test results, 13 (32%) only informed the employer and 5 (12%) only informed the employee. Four (10%) did not respond. It is not known whether results given to the employer were then relayed to the employee.
- The methods of communication varied from telephone, mail, fax, or a combination. Medical supervisors who informed the employee directly also indicated that results were given in person.

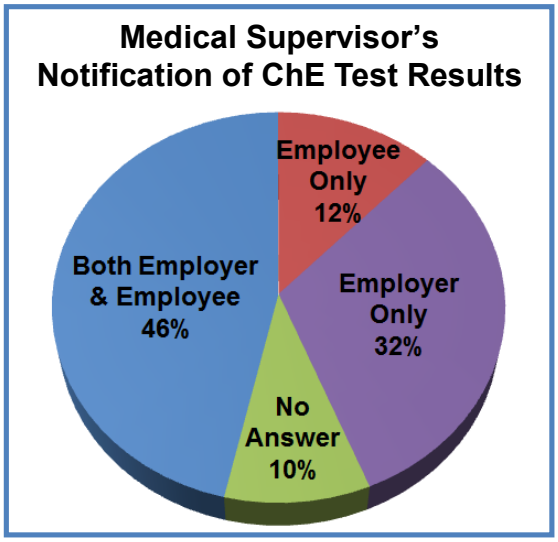


Figure D6: *Person notified by medical supervisor of the ChE test results. (Total number of medical supervisors who responded to the survey, n=41.)*

Table D3: Method by which Employers and Employees are Notified of ChE Test Results

Employee			Employer		
Method	n	%[1]	Method	n	%[1]
Mail	12	38%	Mail	16	30%
Telephone	7	22%	Telephone	12	22%
In Person/Office Visit	7	22%	Email	12	22%
Thru Employer	4	13%	Fax	11	20%
Other, unspecified; only when results are abnormal	1	3%	No Answer	2	4%
No Answer	1	3%	Other, unspecified	1	2%
Total	32	---	Total	54	---

[1] Percentages do not total 100% as respondent may have indicated using more than 1 method to inform patient or employer of ChE test results.

➢ **Interpreting the ChE test and recommendations (Figure D7)**

Interpretation of the ChE test is a medical function. If a worker's ChE levels reach or exceed action levels (≥ 20% for both RBC and plasma ChE depression from baseline), the Program requires the medical supervisor to investigate employee's work practices and modify their work activities until his/her ChE test results are above 80% of baseline levels.

- Nearly all of the medical supervisors interpreted the ChE test results (88%, n=36) and when appropriate, gave the employer recommendations regarding the employee's work activities.
- The same number of medical supervisors (88%, n=36) ordered immediate re-testing until a worker's ChE levels for both RBC and plasma returned to 80% or greater of the baseline.
- Although not required by the Program, the *Guidelines for Physicians* recommends that medical supervisors examine employees for fitness and visit the employee's worksite.
  - ❖ Twenty six (63%) medical supervisors also examined employees for fitness.
  - ❖ Thirteen (32%) medical supervisors visited the employee's worksite.

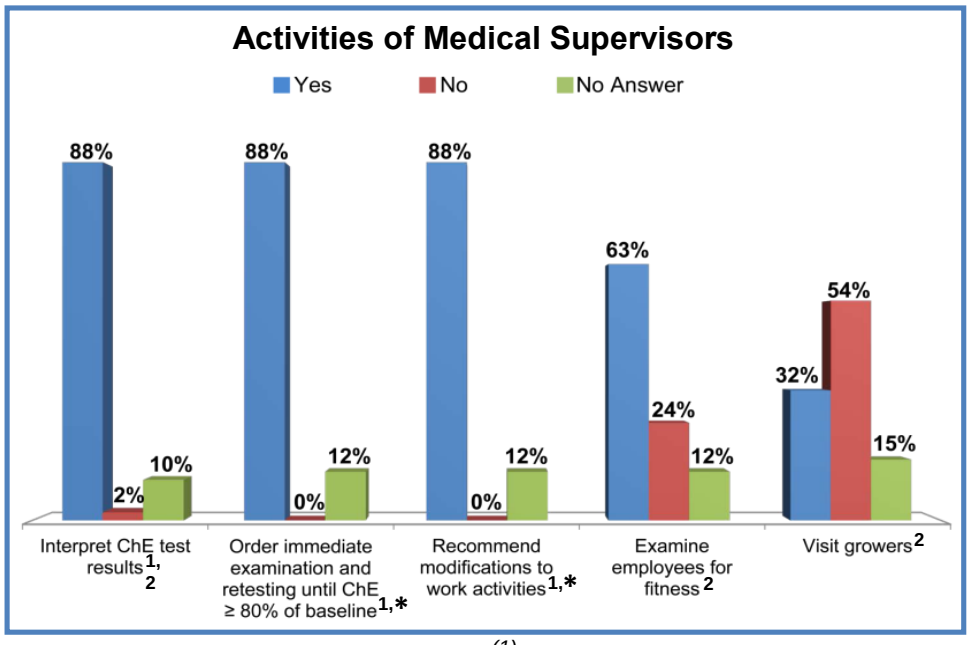


Figure D7: *Program required activities (1) of medical supervisors and those that are recommended in the Guidelines for Physicians (2). (Total number of medical supervisors who responded to the survey, n=41.)*
***** *- When employee's ChE test results reach or exceed action level.*

➢ **Knowledge of follow-through with recommendations (Figure D8)**

The medical supervisors were asked if, and how, they knew that their recommendations were followed.

- Twenty three (56%) medical supervisors reported they learned their recommendations were followed through:
  - ❖ Employer (74%, n=17)

- ❖ Employee (48%, n=11)
- ❖ Personal observation (17%, n=4), or
- ❖ Other methods (e.g., the CAC or Local Health Officer (LHO)) (8%, n=2)

Note: Survey respondents were allowed to choose more than one answer.

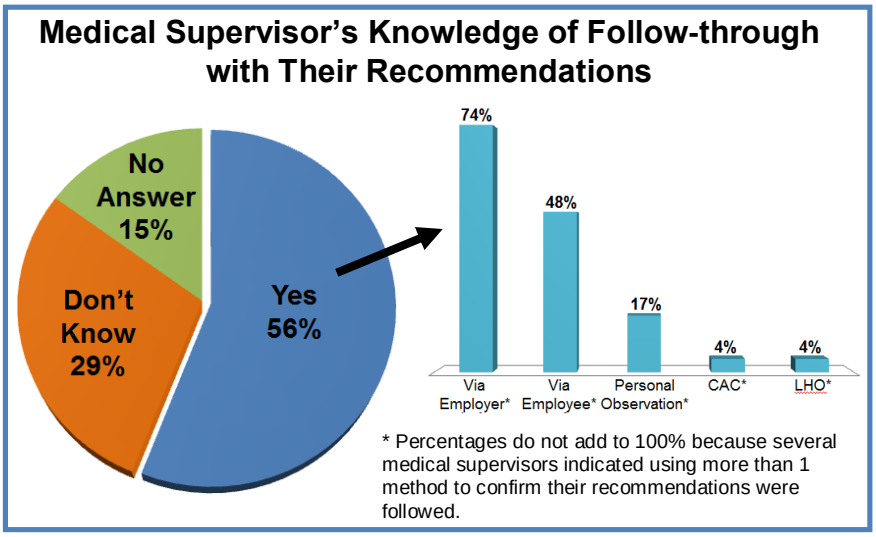


Figure D8: *Knowledge of follow-through with recommendations and method by which medical supervisors learned their recommendations were followed. (Total number of medical supervisors who responded to the survey, n=41.)*

➢ **Obtaining blood sample and laboratory analysis (Figure D9, Tables D4a and D4b)**

The *Guidelines for Physicians* recommends that the medical supervisor submit the employee's blood specimen sample to the same laboratory for analysis.

- Twenty-four (59%) medical supervisors collected the blood specimen from the employee at their clinic or office. Eleven (27%) sent the employee to a drawing laboratory. Two (5%) medical supervisor used both methods. The remaining four (10%) medical supervisors did not provide an answer.

- Of the medical supervisors who collected the employee's blood specimen at their clinic or office:
  - ❖ Thirteen (50%) send the specimen to one of the six laboratories approved by CDPH. Additionally, they stated using the same laboratory consistently for ChE analysis.

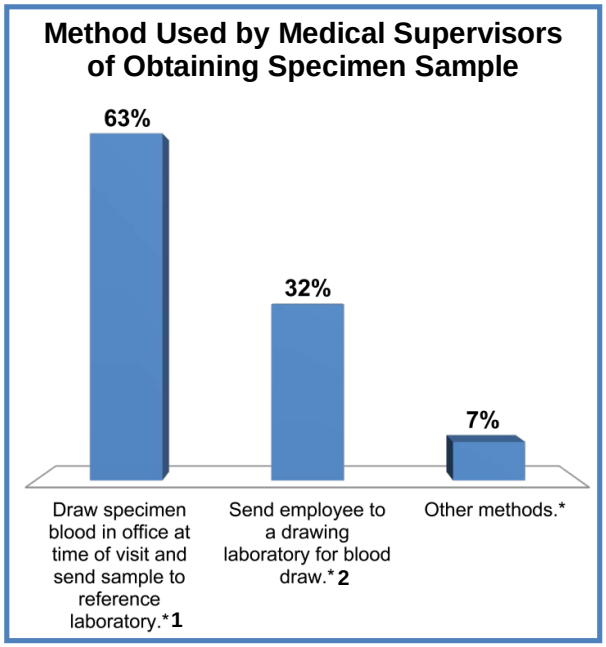


Figure D9: *Method used by medical supervisors to obtain employee's blood specimen for ChE testing. (Total number of medical supervisors who responded to the survey, n=41)*
******* *– Percentages do not total 100% because several medical supervisors indicated more than 1 method for obtaining employee's blood specimen.*
1 *– Three-fourths of these medical supervisors consistently send specimen samples to same reference laboratory.*
2 *– All of these medical supervisors consistently send employees to the same drawing lab.*

- ❖ Four (15%) reported using two different laboratories for ChE analysis. One of these laboratories is not on the list of facilities approved to perform ChE testing for occupational surveillance.
- ❖ One (4%) indicated a drawing laboratory.
- ❖ Eight did not provide an answer.

Table D4a: Laboratories used by medical supervisors for blood specimen analysis[1]

Laboratory	n	%
Quest Diagnostics	15	58%
Medtox/LabCorp	3	12%
PALI	1	4%
PACTOX	1	4%
Pacific Diagnostic Laboratory[2]	1	4%
Adventist Health-LVN[3]	1	4%
No answer	8	31%
Total	30	---

Table D4b: Drawing lab used by medical supervisors to obtain employee's blood.

Laboratory	n	%
Quest Diagnostics	5	38%
Kaiser Permanente Lab	2	15%
Sutter lab	1	8%
Rideout Hospital	1	8%
PALI	1	8%
No Answer	3	23%
Total	13	100%

[1] Percentages do not total 100% because several medical supervisors indicated using more than one laboratory for blood specimen analysis.

[2] Not approved by CDPH to perform ChE test analysis for medical supervision program.

[3] Adventist Health is a drawing laboratory. The medical supervisor indicated that the blood specimen is obtained at time of office visit and reported sending the blood specimen to this laboratory. He did not indicate if the employee is sent to a drawing laboratory to obtain specimen blood.

➢ **Indicating the Purpose of the ChE test on the laboratory requisition slip (Figure D10).**

HSC §105206 requires medical supervisors to include the purpose of the test when ordering ChE testing. This information is required in the electronic reports submitted by the laboratories.

- Twenty-one (51%, n=21) medical supervisors indicated the purpose of the ChE test when ordering it while 13 (32%) did not. Seven (17%, n=7) did not answer this question.
- The reasons given by the 13 medical supervisors for not indicating the purpose of the ChE test were:
  - ❖ They were unaware of this requirement (46%, n=6).

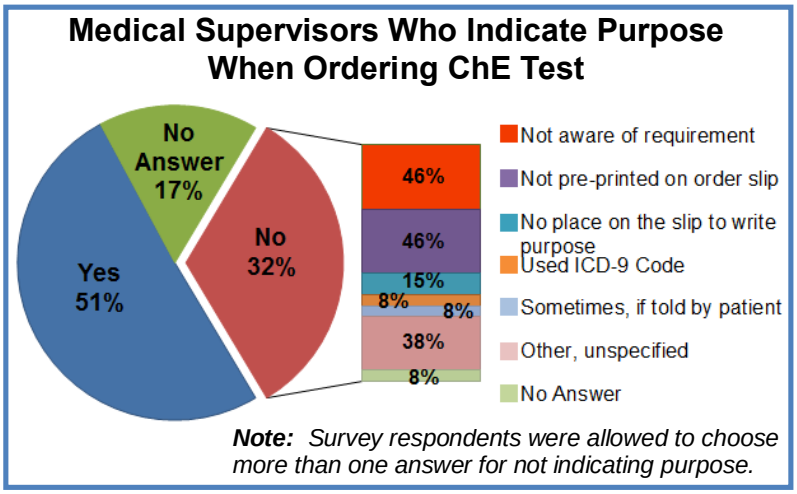


Figure D10: Figure 17: *Number of medical supervisors who indicated purpose of test when ordering ChE test and reasons for not indicating for those who do not indicate purpose of test. (Total number of medical supervisors who responded to the survey, n=41.)*

- ❖ The "purpose" of the test was not pre-printed on the laboratory requisition slip (46%, n=6).
- ❖ There was no room on the order slip to indicate the purpose of the test (15%, n=2).
- ❖ Other, unspecified reasons (38%, n=5).

➢ **Training for Medical Supervision (Figure D11a and D11b)**

The Program requires that medical supervisors have a copy of "*Medical Supervision of Pesticide Workers – Guidelines for Physicians*" and be aware of its contents.

- Thirty (73%) medical supervisors indicated they are familiar with this document.
- Six (15%) medical supervisors reported they have attended a Medical Supervision Training class.
- Ten (24%) medical supervisors indicated they do not remember having attended a Medical Supervision Training class.
- Twenty-one (51%) of the medical supervisors reported they have not attended a Medical Supervision Training class.

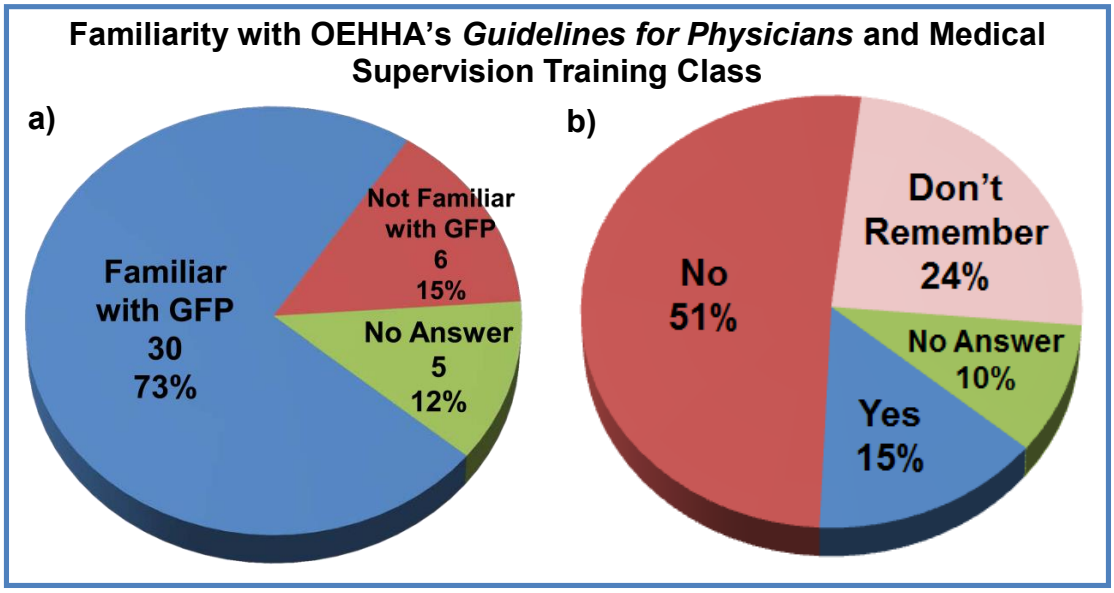


Figure D11: a) *Number of medical supervisors who indicated familiarity or not with the Guidelines for Physicians.* ***b)*** *Number of medical supervisors who indicated they have attended a medical supervisor training class or not. (Total number of medical supervisors who responded to the survey, n=41.) GFP: Guidelines for Physicians.*

Summary of Findings from the Medical Supervisor Survey

Finding 1: We suspect that approximately 70% of the ChE test results submitted by the laboratories are probably unrelated to occupational health surveillance that are under the Program (Figure C22 from Appendix C). Of the 1,021 names entered as the 'ordering physician' in the ChE test reports, DPR verified that only 699 are licensed physicians. We could not determine the occupation for 200 names. The remaining 120 names were: a) not medical doctors, b) supposedly physicians but their license could not be verified, or c) were deceased. During the verification process, we came across two occupational health physicians who work

with non-agricultural employees (e.g., Department of Toxic Substance Control and HazMat employees). While performing follow-up calls, we spoke with physicians who confirmed they have submitted blood specimen samples for ChE analysis for occupational purposes but not for the Program.

Finding 2: Most of the physicians surveyed were aware of their responsibilities as a medical supervisor, although they had varying degrees of understanding of specific requirements.

- Three-fourths of the medical supervisors obtain baseline ChE tests for new hires, however, only 54% indicated they perform periodic testing.
- Half of the medical supervisors indicated the purpose of the ChE test when ordering it. One of the main reasons medical supervisors provided for not indicating purpose was that they were unaware of this requirement.
- A third of all medical supervisors gave the ChE test results to the employers. However, it is unclear if these results were relayed to the employees.
- While nearly all of the medical supervisors made recommendations when the employee's ChE levels reached action level, only 56% knew if an employer followed the recommendations.
- Although most medical supervisors were familiar with the *Guidelines for Physicians*, few (15%) have attended a Medical Supervisor Training class. Training provides the physician with the knowledge necessary to properly implement the Program.
- Based on the telephone call surveys, some physicians who managed pesticide related illnesses in agricultural workers were not necessarily medical supervisors. They were not aware that a state ChE monitoring program exists. These physicians (15%, n=6) thought they 'could be medical supervisors', but were unclear on what this entails.

Finding 3: A medical supervisor's ability to indicate the true purpose of a ChE test, and for the laboratories to capture and report this information, is limited by the current test ordering structure.

- Although half of the medical supervisors we identified in our survey reported that they indicate the purpose of the ChE test when ordering it, numerous submitted ChE test reports continue to have vague entries entered as the purpose of the test. These are difficult to interpret in relation to the workers' activities (Table B2e in Appendix B).
- The survey suggests that laboratory requisition slips are essential in capturing the necessary information to adequately evaluate the Program. One of the main reasons medical supervisors gave for not indicating the purpose of the ChE test is that there is no designated place on the requisition slip to provide this information.
    - All six laboratories have the ability to customize their requisition slips or electronic ordering interfaces based on client's needs. However, for them to modify their requisition slips to include ChE test types and purpose, the request must be initiated by a physician or healthcare provider. The following are minor modifications made by laboratories to their requisition slips based on clients' requests:
        - ❖ ARUP and MEDTOX requisition slips allow specifying a ChE test but not the purpose of the test (Figures D12a and D12b).

- ❖ In 2014, PALI and PACTOX modified their requisition form to reflect the ChE test purpose (Figures D12c and D12d). However, the physician will need to request this modification and check the appropriate test purpose when submitting a ChE test order.
- ❖ In 2013, QDI laboratories in San Juan Capistrano included "Ask and Order Entry (AOE)" questions on their online test order interfaces. This prompts the ordering physician to specify, in their own words, the purpose of the ChE test that is automatically included in their reports to DPR. QDI followed suit in 2014.

- Despite the modifications made by some laboratories to their requisitions slips, this has not improved reporting the true purpose of the ChE tests submitted to DPR.

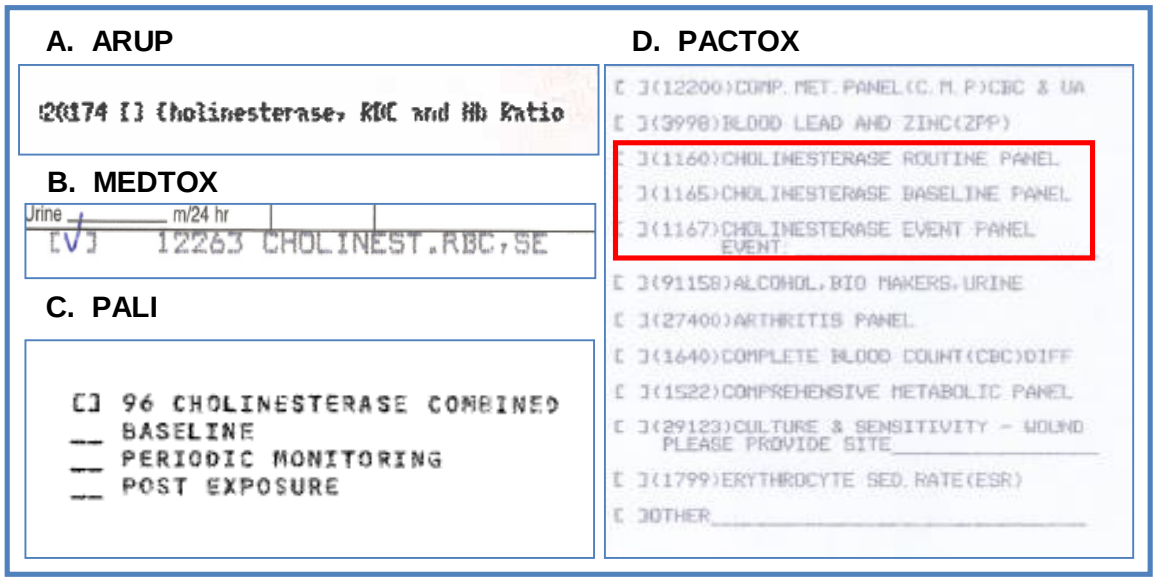


Figure D12: *Examples of ChE test orders on laboratory requisition slips based on clients' requests.*

- HSC §105206 requires that laboratories, not the medical supervisor, report ChE test results to DPR. This schema works on the assumption that the medical supervisor provides all the information related to the test he/she ordered, including the purpose of the test to the laboratory. The laboratory then simply has to report this information and the ChE test results to DPR. Regardless of how a physician orders a ChE test, the purpose of the test has to be clearly conveyed to the laboratory to be included in the reports. While preparing for the distribution of the survey, we discovered that nurses, physician assistants, medical assistants, and office managers may be ordering the ChE tests. These persons may or may not be aware of the Program or reporting requirements.

- While reporting most of the data elements required by HSC §105206 is straightforward, clearly conveying the purpose of the ChE test is more complicated. It works on the premise that the employer, medical supervisor, their staff, and the drawing and/or reference laboratories all have a clear and consistent understanding of what is meant by the true purpose of a ChE test as it relates to the patient's work

activities handling OPs/CBs. This premise may not be entirely correct based on the reports DPR has received.

- The medical supervisor needs to provide ALL the information required by HSC §105206 to the laboratory so that they are relieved of the burden of having to determine the true purpose of the ChE test.

- Currently, a structure does not exists that allows (1) a medical supervisor to include all the data elements required by HSC §105206 in their test orders, and (2) a laboratory to extract this information from test orders and report this information, along with the test results, to DPR. Unless information through electronic orders or on laboratory requisition slips is captured by the laboratories, it will be challenging to effectively evaluate the Program based solely on the ChE test results.

Unless improvements are made to the way pertinent information is transferred from the medical supervisors to the laboratories, and how the laboratories report this information to DPR, we will continue to receive data that does not accurately reflect the Program.

Department of Pesticide Regulation

Brian R. Leahy
Director

Edmund G. Brown Jr.
Governor

April 24, 2014

<First name> <Last name>, MD
<address>
<City>, <State> <zip>

Re: Questionnaire for Medical Supervisors contracted with growers or businesses where agricultural workers handle cholinesterase-inhibiting pesticides.

Dear Dr. <Last name>:

In accordance with Title 3 of the California Code of Regulations Section 6728 **Medical Supervision (3CCR 6728), employers are required to provide medical supervision for** employees who regularly mixes, loads, or applies pesticide with the signal word "DANGER" or "WARNING" that contains an organophosphate or carbamate, for the commercial or research production of an agricultural plant commodity for more than 6 days in any 30 consecutive days in order to monitor for exposure. To meet the requirements of this regulation, a medical supervisor orders red blood cell and plasma (or serum) cholinesterase tests at a laboratory approved by the California Department of Public Health (CDPH), and interprets the test results for cholinesterase (ChE) activity.

The California Health and Safety Code (HSC)105206 requires laboratories that are approved by CDPH to perform cholinesterase testing for occupational health surveillance to report specific information on employees under the Medical Supervision program to the Department of Pesticide Regulation (DPR). The same requirement also applies to persons who have had a suspected or known exposure to pesticide containing cholinesterase inhibitors. DPR may share the information electronically with the Office of Environmental Health Hazard Assessment (OEHHA) and the California Department of Public Health (CDPH). In addition to the tested person's name, date of birth, and the medical supervisor's name, address and telephone number, HSC 105206 also requires laboratories to indicate the **"purpose of test"** on the cholinesterase test results reported to DPR. Reporting laboratories can only include **"purpose of test"** in their reports when an ordering Medical Supervisor has indicated such on the laboratory requisition slip. The Medical Supervisor must indicate whether the **"purpose of test"** is for establishing a worker's **baseline** Cholinesterase level, for routine Cholinesterase **monitoring**, or an **event** to evaluate suspected pesticide illness. These requirements are specified in the HSC 105206, subsection (c).

1001 I Street • P.O. Box 4015 • Sacramento, California 95812-4015 • www.cdpr.ca.gov

A Department of the California Environmental Protection Agency

<First name> <Last name>, MD
April 24, 2014
Page 2

You are receiving this letter because you ordered blood Cholinesterase tests from a laboratory approved by CDPH to perform cholinesterase testing for occupational health surveillance. The results of these tests were reported to CDPR under HSC 105206. We request a few minutes of your time to complete the attached questionnaire. Your cooperation is crucial in our effort to evaluate the effectiveness of the Medical Supervision Program for agricultural workers as specified in 3 CCR 6728. Please mail the completed questionnaire in the enclosed self-addressed stamped envelope by May 23, 2014. If we do not receive the completed questionnaire, please expect a follow-up call from either Drs. Lucy Graham or Yvette Nonato in order to help you complete the questionnaire by phone.

If you have any questions on the questionnaire or the cholinesterase reporting requirements, please feel free to contact us.

Thank you for your attention.

Sincerely,

Saturnino Yanga, DVM, MPVM, MS
CDPR/Worker Health and Safety Branch

Encl.

The complete text of 3CCR 6728 (Medical Supervision) can be viewed at http://www.cdpr.ca.gov/docs/legbills/calcode/030302.htm#a6728.

The complete text of HSC 105206 can be viewed at http://leginfo.legislature.ca.gov/faces/codes_displaySection.xhtml?lawCode=HSC&sectionNum=105206.

QUESTIONNAIRE for Medical Supervisors
Please PRINT legibly

First Name: _____ **Last Name**: _____

Please check appropriate box: ☐**MD** ☐**DO** ☐**PA** ☐**NP** ☐Other, please specify _____

Type of practice: ☐Occupational Medicine ☐Family Practice ☐Internal Medicine

☐Other, please specify: _____

Clinic/Hospital/Affiliation:

Complete address: _____

Telephone: (___)_____ **Email:**

1. Are you *currently* a Medical Supervisor contracted with a grower or company to supervise *agricultural* workers handling Cholinesterase (ChE) inhibiting pesticides?
   ☐**Yes** ☐**No**

   *If **YES**, please proceed to question 3. If **NO**, please proceed to question 2.*

2. Were you a Medical Supervisor contracted with a grower or company to supervise *agricultural* workers handling ChE inhibiting pesticides from 2011 to 2013?
   ☐**Yes** ☐**No**

   *If **YES**, please proceed to question 3.*

   *If NO to questions 1 **and** 2, **STOP** here. Please insert the questionnaire in the self-addressed stamped envelope and **mail it to us.** Thank you for your time.*

3. Have you attended a training class in medical supervision?
   ☐**Yes** ☐**No** ☐**Don't remember**

4. When you order Blood Cholinesterase (ChE) tests for pesticide handlers, do you indicate the ***"purpose of test"*** on laboratory requisition slips (i.e., **BASELINE** to establish ChE levels, **MONITORING** for routine ChE testing, or **EVENT** in cases of pesticide exposure)?
   ☐**Yes** ☐**No**

   If NO, it is because:
   a. The purpose was not pre-printed on the lab requisition slips. ☐**Yes** ☐**No**
   b. There was no place on the lab requisition slip to write in the purpose. ☐**Yes** ☐**No**
   c. I was not aware of this requirement. ☐**Yes** ☐**No**
   d. Other: _____

5. How do/did you obtain employee's blood sample for ChE test analysis?

a. Draw specimen blood in office at time of visit *and* send sample to laboratory. ***If no**, proceed to 5b.* ***If yes***, name of laboratory:_____	☐**Yes** ☐**No**

Please continue on the other side.

Do/did you send the employee to this same laboratory for every ChE test ordered? ***If no***, name of laboratory(ies):_____	□**Yes**	□**No**
b. Send employee to a clinical laboratory for blood draw. ***If no, proceed to 5c.*** ***If yes***, name of laboratory:_____	□**Yes**	□**No**
Do/did you send the employee to this same clinical laboratory for blood draw? ***If no***, name of laboratory(ies):_____	□**Yes**	□**No**
c. Other methods. Please specify.		

6. Do/Did you or Are/Were you *(please answer each question)*:

Familiar with OEHHA's Guidelines for Physicians?	□**Yes**	□**No**
Visit the grower or employee's worksite?	□**Yes**	□**No**
Examine employees for fitness?	□**Yes**	□**No**
Obtain baseline ChE test for new hires?	□**Yes**	□**No**
Obtain baseline ChE test every 2 years?	□**Yes**	□**No**
Obtain routine ChE tests for employees once every 60-day period? ***If not***, how often do you order routine ChE tests? Every ____ days	□**Yes**	□**No**
Obtain ChE tests in the event of a pesticide exposure?	□**Yes**	□**No**
Interpret ChE tests results?	□**Yes**	□**No**
Informed of the number of days an employee handled ChE-inhibiting pesticides within a 30-day period? ***If yes***, who informed you? ☐Employee ☐Employer	□**Yes**	□**No**
Inform employee of ChE test results? ***If yes***, by what method? ☐Telephone ☐Mail ☐Email ☐Other: _____	□**Yes**	□**No**
Give ChE test results to employers to relay to employee? ***If yes***, by what method? ☐Telephone ☐Mail ☐Email ☐Other: _____	□**Yes**	□**No**
Report pesticide-related illness to your local health officer as required by HSC 105200?	□**Yes**	□**No**

7. When an employee's ChE test results show a depression of >30% (RBC) or >40% (plasma), do/did you *(please answer each question)*:

Recommend to employer that employee be removed from handling ChE inhibiting pesticides?	□**Yes**	□**No**
Order immediate examination and retesting until enzyme activity levels have returned to 80% or greater of baseline values (RBC and plasma)?	□**Yes**	□**No**

Please continue on next page.

8. Does/did the employer comply with the recommendations you had given in relation to an employee's Cholinesterase (ChE) test results?

☐**Yes** ☐**No** ☐**Don't Know**

If YES, how do/did you know?

From: ☐ Employee feeback ☐ Employer feeback
☐ Agricultural Commissioner ☐ County Health Officer
☐ Personal Observation ☐ Other: _____

9. What grower(s) or company(ies) do/did you have a contract with as a Medical Supervisor?

Company: _____

Contact person: _____

Address: _____

Telephone: _____

Company: _____

Contact person: _____

Address: _____

Telephone: _____

Company: _____

Contact person: _____

Address: _____

Telephone: _____

Please PRINT legibly in the space below if you need to provide information on more contracts.

Thank you for your time. Please return questionnaire using the self-addressed, stamped envelope and mail back to us before ***May 23, 2014***. If you have any questions regarding this questionnaire, please contact Dr. Yvette Nonato at 916-445-2174 or Dr. Lucy Graham at 916-445-4190.

Appendix E: MEDICAL SUPERVISOR IN-PERSON VISITS

In 2015, OEHHA initiated a series of in-person visits with medical supervisors and other health care providers who order ChE tests for the Medical Supervision Program ("Program") throughout California. The goals of the visits were:

1. Provide the physician (medical supervisor) with a copy of the recently revised *Guidelines for Physicians* (OEHHA, 2015) and copy of the latest edition of Recognition and Management of Pesticide Poisonings (USEPA, 2013).
2. Remind the physician of the requirements of HSC §105206, established in 2011:
    - The purpose of the ChE test must be indicated on the laboratory test requisition.
    - The person tested must receive a copy of the test results and any recommendations from the medical supervisor within 14 days of the medical supervisor receiving the test results.
    - Physicians in California must indicate the purpose of the ChE activity test if it is ordered to confirm a possible case of pesticide illness due to a ChE-inhibiting pesticide.
3. Review the responsibilities of the physicians in the Program and provide them with one summary of the essential steps of the Program.
4. Remind physicians that they must have a written agreement with each employer in order to provide medical supervision services.
5. Ask the physician about the process he/she uses to order ChE tests (electronically or with hard copy laboratory slips), and if the purpose of the test could be indicated on the form they use.
6. Determine approximately how many of the ChE tests that the physician orders each year are for the purpose of complying with the Program.
7. Ask the physicians if they have any suggestions to improve the Program and answer any questions about the Program.
8. Inform physicians about OEHHA's medical supervision education and training resources, as outlined in a brochure provided to physicians during the visits.

The visits usually required about 15-30 minutes to complete. A list of the names of medical supervisors was generated from multiple sources, including information reported to DPR on the ChE test results in 2011-2014, responses to the questionnaire survey mailed by DPR to potential medical supervisors in April 2014, the names of medical supervisors provided by their colleagues during the course of visits, and cold calls to clinics specializing in urgent care and industrial or occupational medicine in cities located in major agricultural production areas throughout California.

OEHHA's long-term goal is to contact all healthcare providers who order ChE tests for the Program. For those providers who cannot be interviewed in person, OEHHA will provide them the latest information about the Program by phone and/or mail. We have identified and reached out to 87 physicians. Of these, 79 are currently participating in the program and meet our definition of 'physician medical supervisor' (Figure E1). As of November 20, 2015, 60 health care providers were visited. These included 41 medical supervisors, 8 physician assistants and 3 nurse practitioners who were working under the direction of a medical supervisor. Another

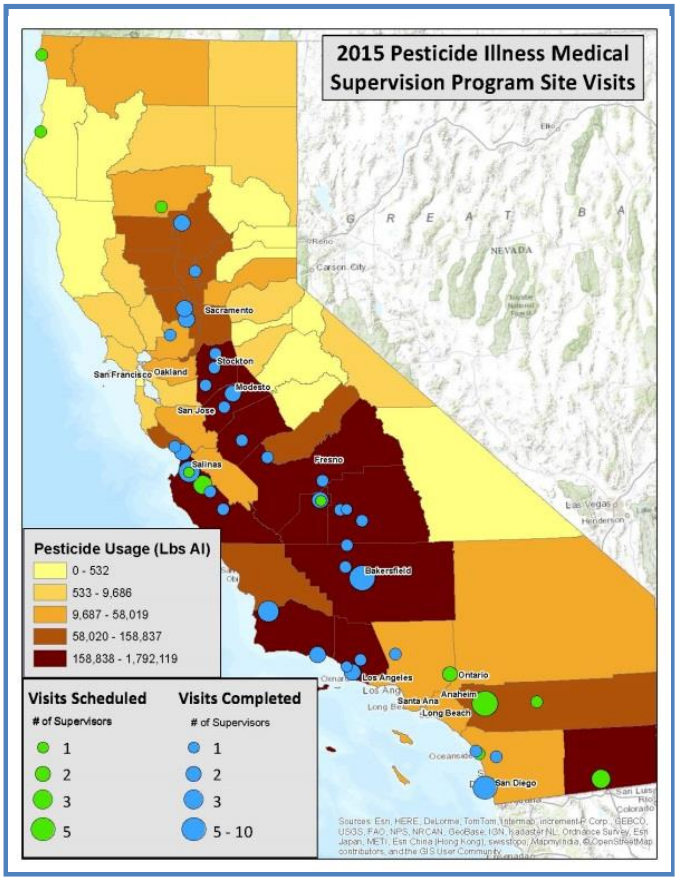


Figure E1: *Geographic distribution of OPs/CBs types I and II used (2011 – 2013), and location and number of in-person visits. (Total number of physicians visited, n=60)*

eight physicians were confirmed not to be medical supervisors in the Program at time of interview. When only physician assistants or nurse practitioners were present at time of in-person visit, the medical supervisors will be contacted by phone for follow-up. Figure E2 summarizes major findings from the in-person visits with medical supervisors (n=41).

A few of the physicians visited were not medical supervisors even though they originally had classified themselves as such in the questionnaire survey. They apparently misunderstood that the survey was specifically referring to California's Medical Supervision Program, not the general supervisory/managerial responsibilities of some physicians. They also may have responded to the survey because they order annual baseline ChE tests for non-pesticide workers such as emergency first responders.
We found that some medical supervisors on our list retired during the 2011-2014 timeframe, and others had just begun to assume the responsibilities of medical supervision. Some medical supervisors who had not completed or received the survey, and hence were not included on the DPR survey list, were identified by their colleagues during the course of the visits or through cold calls. A map showing the locations of the medical supervisors who were interviewed as well as those identified as suspected or likely medical supervisors but not yet confirmed is shown above (Figure E1).

In general, medical supervisors were knowledgeable about the Program (Figure E2c). Most were able to provide a general estimate of the number of ChE tests they ordered each year during the last 3 to 5 years (Figure E2a). Their level of awareness of the Program generally correlated with the number of tests they reported ordering per year. Similarly, medical supervisors working in regions where large amounts of OPs/CBs are used, including California's Central Valley and Salinas Valley, were generally more familiar with their responsibilities than those working in regions with less frequent OPs/CBs use. However, many medical supervisors throughout the state were not aware of and not complying with the new provisions of HSC §105206. They appreciated being told about them and were willing to integrate them into their practice. Many medical supervisors stated they did not have many follow-up tests because their patients most likely did not handle OPs/CBs often enough (Figure E2b). This comment is consistent with one of the primary findings of the growers' headquarters inspections, suggesting that the work activities of OP/CB pesticide handlers were often managed to ensure that the threshold required for follow-up testing (more than six days in a 30-day period) was not

exceeded. Most medical supervisors stated they rarely had follow-up tests that required an employer to take action (review of work practices or removal from any activities that involved OP/CB handling), but if they did, they contacted the employer to discuss test results and make recommendations.

Overall, the medical supervisors visited were very receptive and found the information we provided especially helpful. Three key requests were made by multiple medical supervisors: 1) work with the clinical laboratories to update the requisition slips to include a space to indicate the test purpose, 2) create a downloadable spreadsheet tool for physicians to use to log and calculate changes in patient ChE levels, and 3) post the one-page ChE test reporting and review summary document created by OEHHA, on the OEHHA website so that it is readily accessible.

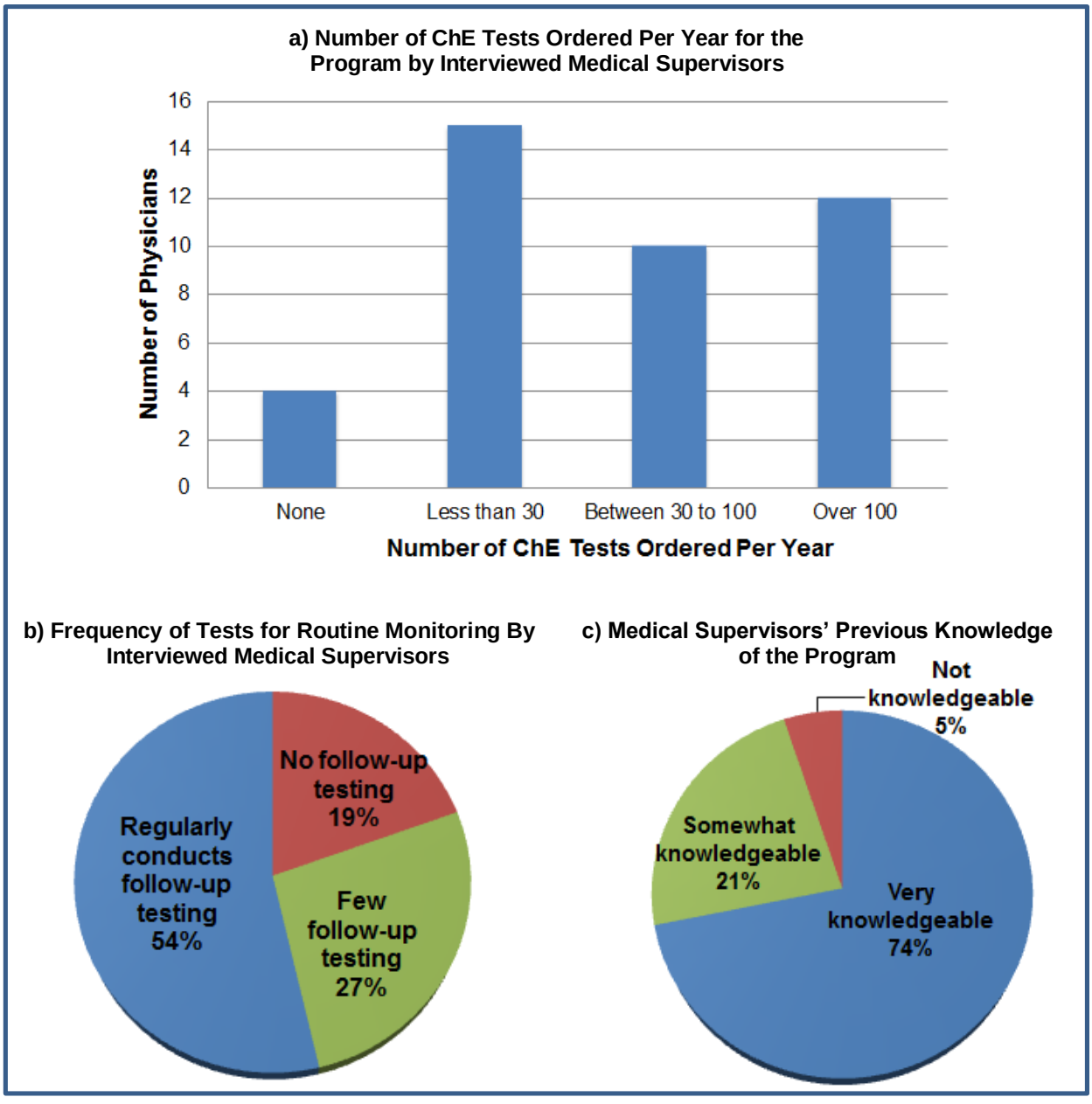


Figure E2: *Major findings from in-person visits. Total number of medical supervisors interviewed, n=41.*

Medical Supervision Program In-Person Visit Checklist

Location: _____ Medical Supervisor: _____

Date: _____ Total time of visit: _____ Other Clinic Staff: _____

Team Members Present (Circle): Chuck Salocks Bill Ngai Suzanne Forsyth
Rebecca Belloso Hana Blatter Other: _____

- ❑ Introduce yourself and those with you- ***OEHHA manages MedSup program***
- ❑ Briefly mention the Medical Supervision Program- ***not an inspection/enforcement visit***
- ❑ How long have you acted as a Medical Supervisor? _____
- ❑ How many health care providers in your clinic participate in the program/order ChE tests/evaluate test results? _____
- ❑ Purpose of Visit- ***Explain why we are here***
    - ❑ Give a copy of the *Guidelines/EPA Pesticides Poisoning* handbook
    - ❑ Physicians are required to have copy of *Guidelines*/be aware of contents
    - ❑ Inform Medical Supervisor of changes to the law- ***SEE GLOSSY***
- ❑ Initial Visit/Establish Baseline
    - ❑ Screen worker- Is employee healthy enough to work with pesticides?
- ❑ Periodic Testing Requirements
    - ❑ What is the process when ordering tests? Does your clinic software/electronic medical record allow you to add comments (indicate purpose of test) when ordering? (Yes / No)
    - ❑ Establish baseline- regulation requires 1 test (***Both RBC and plasma ChE level***)

      OEHHA suggests an average of 2 tests
    - ❑ Cautionary information – Approved labs only/Do not use lab normal values for baseline
- ❑ Test Result Actions and Recommendations
    - ❑ Physician must compare results to the baseline and ***ensure employer and employee*** receive a copy of results and recommendations
    - ❑ Should employee:
        - ***keep working?***
        - ***be removed from work?***
        - ***return to work***?
    - ❑ Frequency of follow ups
        - ❑ Do your patients follow up/come back for second tests? (Yes / No)
        - ❑ How many come back for follow up/secondary testing?

          Approximate number or percent: _____

- ❑ Reminder- Medical Supervisor must have written agreement with employer
- ❑ Program Outreach
    - ❑ What is the best way to reach you and your staff? _____
      _____
    - ❑ How many ChE tests are you ordering per year? _____ How many are for the Medical Supervision program? _____
    - ❑ Do you send the test results/recommendations to the employers? (Yes / No)
    - ❑ Do you feel your recommendation is taken seriously? (Yes / No)
    - ❑ Do you have suggestions for improving the program? (Yes / No) Any concerns?
    - ❑ Direct physician to training resources- ***provide brochure***
    - ❑ (Yes / No) Notes: _____
      _____
      _____
      _____
    - ❑ Do you have any questions? (Yes / No) Notes: _____
      _____
      _____
      _____

Cholinesterase Testing for Monitoring Workers in the California Medical Supervision Program

1. **SCREEN THE WORKER** on the initial visit to be sure he/she can work with cholinesterase inhibiting pesticides.

2. **ESTABLISH BASELINE** cholinesterase activity levels *before* follow-up testing.
   - One test is required by regulation and consists of measuring RBC cholinesterase **AND** plasma cholinesterase **(*not* one or the other**).
   - Average of two tests is recommended by OEHHA. Details in *Guidelines*.
   - **Do not use lab normal values for baselines.**
   - Always put blood samples on ice or store at 4°C immediately after drawing.

3. **LAB.** Only use a California Department of Public Health certified lab listed at: http://www.cdph.ca.gov/certlic/labs/Documents/CHE%20LAB%20list%2001012007.pdf

4. **INDICATE PURPOSE OF THE TEST** on the lab slip when ordering a cholinesterase activity test for this program. Use one of the following terms:

   Baseline, Follow-up, or Recovery

5. **FOLLOW-UP TESTS** as required.
   - Once every 30-day qualifying period for first 3 follow-up tests.
   - If no problems detected, then at least once every 60 days (two 30-day qualifying periods) unless otherwise recommended by the physician.
   - More frequent testing is at the discretion of the physician.

6. **COMPARE FOLLOW-UP RESULTS TO THE BASELINE LEVELS** to evaluate for inhibition of cholinesterase and make recommendations, including:

Percent of Baseline Activity	RBC ChE	Plasma ChE
<80%	Prompt retesting of employee and evaluation of work practices by employer	
≤70%	Immediate removal of employee from further exposure	-
≤60%	-	Immediate removal of employee from further exposure

Provide a copy of test results and recommendations to the employer.

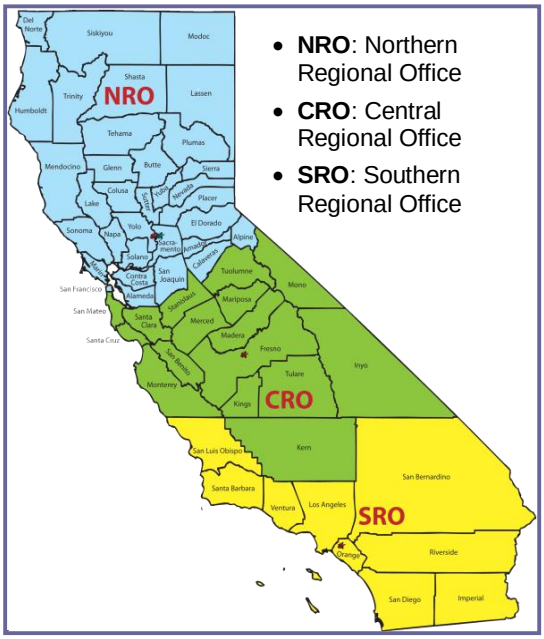
7. **INFORM WORKER OF RESULTS**. Must ensure that the tested worker receives a copy of the test results and any recommendations from the medical supervisor within 14 days of the medical supervisor receiving the results.

8. **RETURN TO WORK**. Determine when a worker removed from further exposure to these pesticides can resume working with them.
   - When cholinesterase activity levels return to ≥ 80 percent of *both* RBC and plasma cholinesterase baseline values

Appendix F: FOCUSED GROWERS' HEADQUARTERS INSPECTION

From August to December 2014, scientists from DPR conducted focused growers' headquarters inspections to further evaluate the Program. These inspections were intended to:

- Evaluate the grower's awareness of, and compliance with, the Program.
- Evaluate the grower's understanding of his or her role, and responsibilities as an employer in the Program.
- Identify medical supervisors contracted by the grower.



- **NRO**: Northern Regional Office
- **CRO**: Central Regional Office
- **SRO**: Southern Regional Office

Figure F1: *County distribution of DPR's three regional offices.*

DPR used the Pesticide Use Reporting database to identify, at minimum, two counties from each of DPRs three regional offices (Figure F1) that used the most OP/CB from 2010 to 2012. Some County Agricultural Commissioner's (CAC) offices provided additional data on the use of OP/CB applied in their counties in 2013 and 2014. Seven counties were identified for inspections: Butte, San Joaquin, Tehama, Fresno, Tulare, Imperial, and San Diego. Seventy-five percent (75%) of the growers within these counties who use OPs/CBs (identified thru the PUR database) were randomly selected for a headquarters inspection. The regional distribution of the inspected growers is shown in Figure F2. The inspections included interviews and review of records retained by growers. A questionnaire was used to standardize the interviews and to focus on key areas of the Program (see page 106).

Observations were recorded as:

- **In COMPLIANCE** (if the regulatory requirement was met by the grower),
- **NOT in COMPLIANCE** (if the regulatory requirement was NOT met by the grower), or
- **NOT REQUIRED** (if the grower did not meet the criteria for "regularly-handling" OP/CB)

Results of the Focused Headquarters Inspection

Of 83 growers who reportedly used OPs/CBs, 71 (86%) were confirmed to have used these pesticides. The remaining 12 growers were found to have erroneously reported OP/CB use. Of the 71 growers, 26 (37%) had employees that met the Program criteria for regularly handling OPs/CBs. These growers were required to have a medical supervision program (Figure F2).

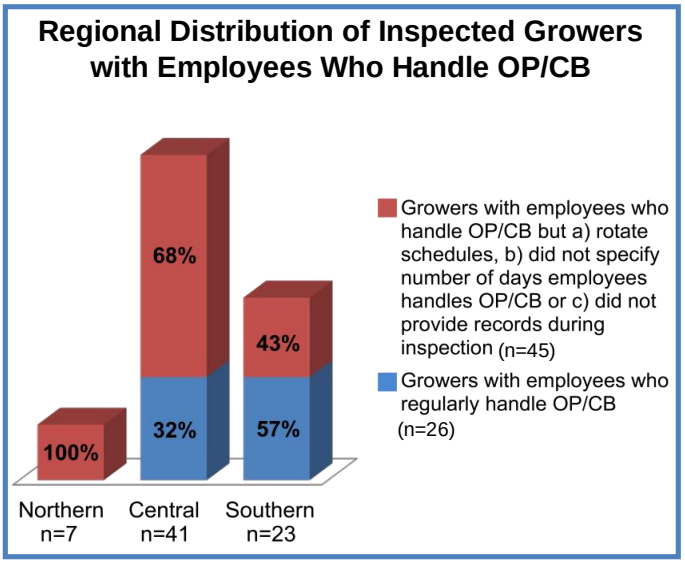


Figure F2: *Number of growers with employees who handle OP/CB by region. "Regularly handle" is defined as handling pesticides more than six days in any 30-day period.*

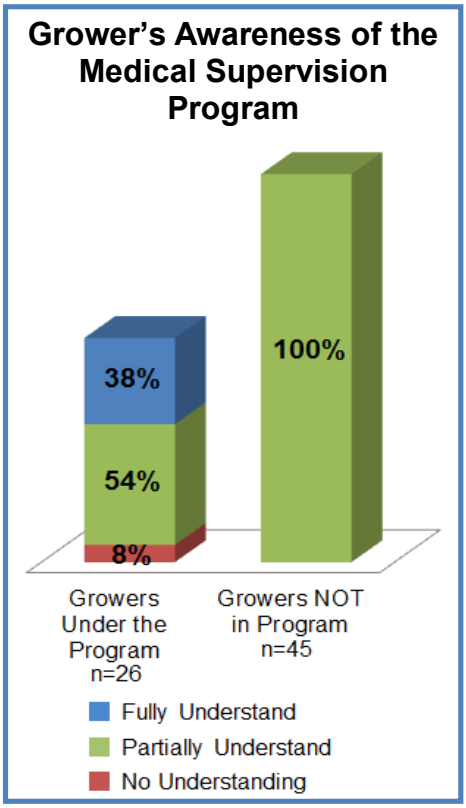


Figure F3: *Grower's level of understanding of the Program. (n=71)*

The headquarters inspections focused on the compliance of the growers to specific aspects of 3CCR §6728. Over half of the growers inspected were familiar with the Program but had varying levels of understanding of the specific requirements (Figure F3).

We limited our analysis to the 26 growers that had employees who regularly handled OP/CBs. Of these, 24 (92%) were aware of the Program (Figure F4).

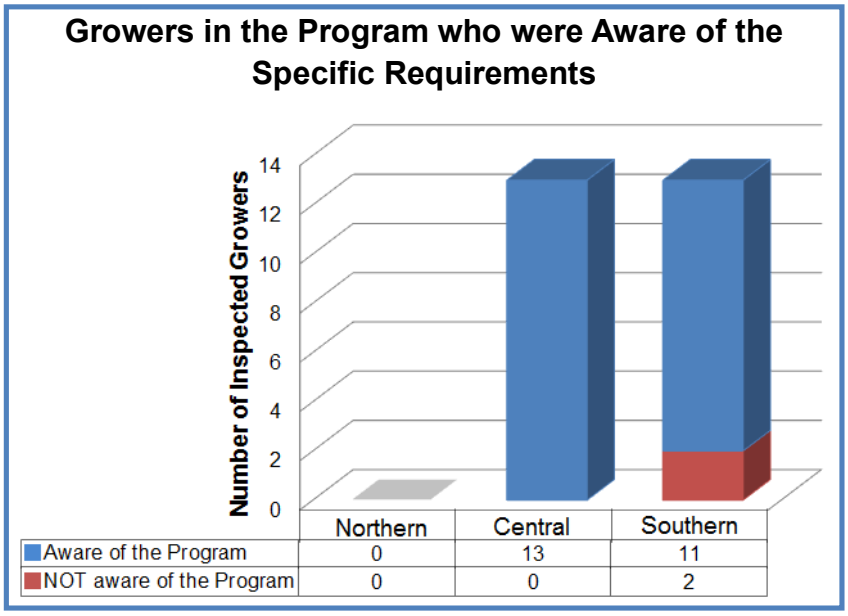


Figure F4: *Number of growers that are in the Program who were aware of the specific requirements by region. (n=26)*

There were 45 growers whose employees did not meet the Program criteria:

- Forty-four (98%) growers had employees who worked with OP/CB but did not meet the criteria for regularly handling these pesticides.
  - ❖ Twenty seven (62%) growers were from the central region and indicated that they put their handlers on a rotation schedule to limit the number of days a handler worked with OP/CBs to less than six days in a 30 day period.
  - ❖ Ten (23%) growers were from the southern region and seven (16%) from the northern region indicated that they did not have employees who regularly handled OPs/CBs. These growers did not specify the actual number of days their employees worked with OP/CBs.
- Only one (2%) grower explicitly stated that none of his employees regularly handled OP/CBs.

The Program requires employers to retain copies of the medical supervisor agreement and their recommendations, the employee's use records, and the ChE test results. In addition, employers are also required to investigate employee's work practices and modify their work activities if his/her ChE test results meet or exceed action levels.

- A majority of the 26 employers (58%, n=15) had the written agreement with the medical supervisor at their office (Figure F5).
- Ten (38%) provided the CAC a copy of the agreement (Figure F6).
- Eleven (42%) retained employee ChE test results and medical supervisor recommendations (Figure F7).

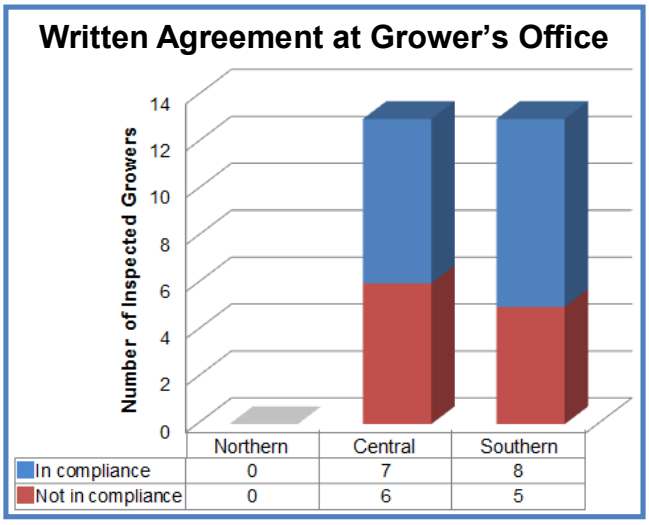


Figure F5: *Number of growers in the Program who had a copy of written agreement with a medical supervisor in the office. (n=26)*

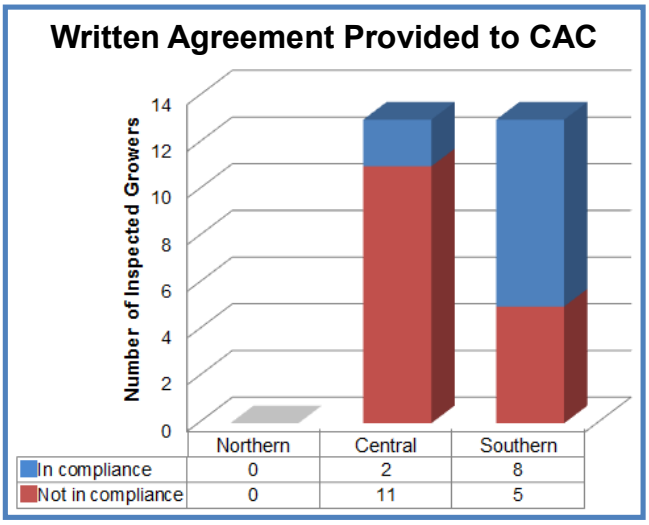


Figure F6: *Number of growers in the Program who provided a copy of written agreement with a medical supervisor to CAC. (n=26)*

The Program is designed to assist the employer in protecting the worker from excessive exposure to OPs/CBs. When an employee's RBC or plasma ChE level meet or exceed the action threshold (≥ 20% for both RBC and plasma ChE depression from baseline), the employer is required to investigate the employee's work practices and modify their work activities until his/her ChE test results are above 80% of baseline levels.

- One grower (4%) had an employee whose ChE results were below the threshold (Figure F8). This grower was notified by the medical supervisor that his employee's ChE test results were physiologically low. The grower not only investigated the employee's work practices but also modified the employee's work duties. We do not know this employee's handling history or previous ChE test results.
- The remaining 25 growers (96%) had employees who had their ChE measured but since their ChE levels results were within normal range, no further action was required (Figure F8).
- A majority of the growers (65%, n=17) indicated that they inform their employees of their ChE test results (Figure F9).

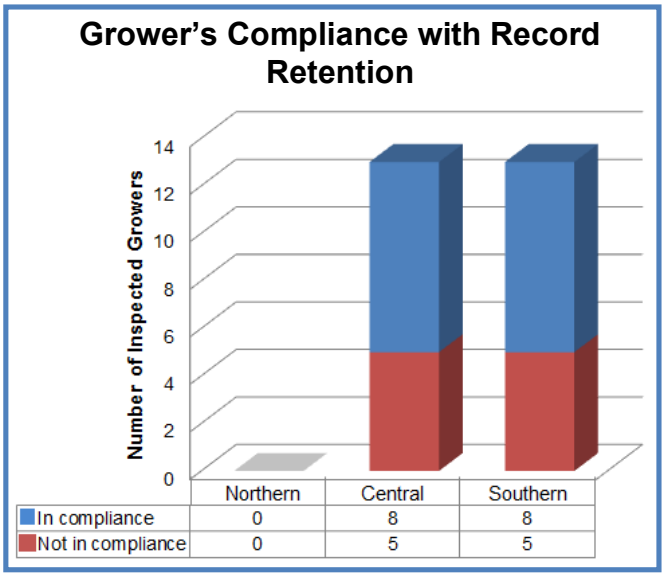


Figure F7: *Number of growers in the Program who retained employee's ChE test results and medical supervisor recommendations. (n=26)*

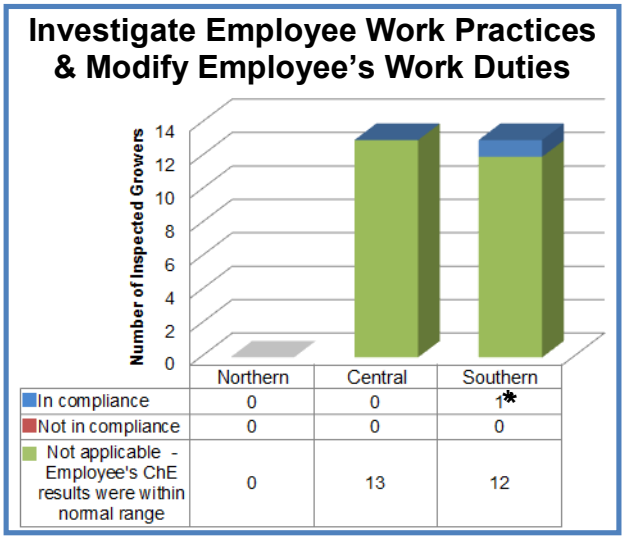


Figure F8: *Number of growers in the Program who investigated employee work practices and modified employee's work duties based on recommendation from medical supervisor. (n=26)*
** - This employee's ChE test results were physiologically low.*

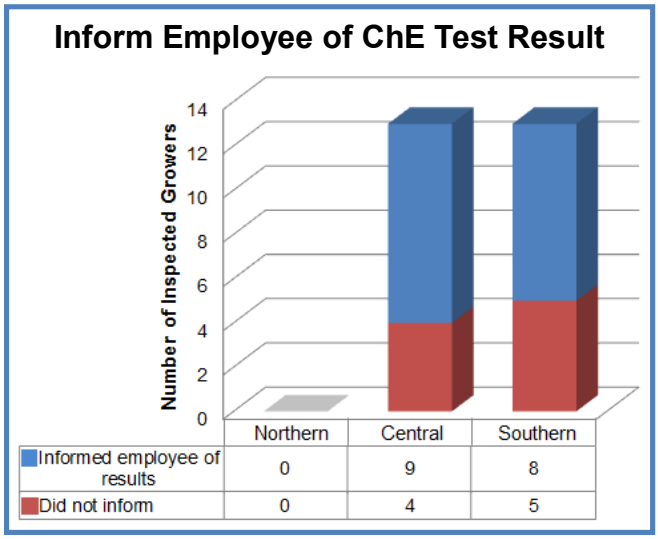


Figure F9: *Number of growers in the Program who informed employee of his/her ChE test results. (n=26)*

Summary of Findings of the Focused Growers' Headquarter Inspections

Finding 1- Nearly all of the growers (92%, n=65) inspected indicated they have heard of the Program. However, improvements can still be made to increase their awareness of the Program. Growers under the Program were either fully or partially aware of the Program. Those not in the Program, may not fully understand the intent of the Program. Some growers

did not have employees who regularly handle OPs/CBs, but followed some of the Program requirements. Three of these growers contracted with a medical supervisor. Another grower said that his employees' baseline ChE levels were obtained every two years. One grower has his employees tested every 30 days. Another grower, who was not aware of the Program, stated that he would immediately send his employees for ChE testing following the headquarters inspection. This grower did not have employees who regularly handled OP/CBs.

Finding 2- Although most of the growers in the Program were aware of the Program, they may not fully understand some of its specific requirements. These requirements include having copies of the medical supervision agreement in their office and with the CAC, and record retention. Seven growers did not keep employee records while one grower said that he had moved his records to another location and could not locate them. One grower stated that their handlers also work at another farm which they own but could not provide the employee's schedule at the other farm.

Growers stated that their medical supervisor provides them with an interpretation of the ChE results. Most growers indicated that they inform their employees of their test results despite not being a Program requirement. However, one grower stated that he only informs an employee of his/her ChE test results if asked for it. Another grower, who said that he had difficulty obtaining the ChE test results from the medical supervisor, assumed that if he did not hear from the medical supervisor, this meant his employee's ChE levels were within normal range.

Finding 3- We are unable to identify all medical supervisors in California. We assumed that the ChE results from the laboratories would give us the names of active medical supervisors beginning in 2011. The focused headquarters inspections generated names of 20 medical supervisors. Eighteen of the 20 names were already on our list of licensed physicians who had been mailed a Medical Supervisor Survey. Fifteen of these physicians were already confirmed Medical Supervisors via our survey. We called the remaining three physicians who were sent a survey but did not respond: one indicated he had retired; one indicated he did not know if he was a medical supervisor although said he sees agricultural workers; and, one did not respond to our calls. The focused headquarters inspection yielded only two new medical supervisors located in the central and southern regions.

Focused Growers' Headquarters Inspection Form, 2014

DPR MEDICAL SUPERVISION SURVEY
Employer Requirements

Reference Number: _____ Interviewer(s): _____

County: _____ Date: ____/____/____ Interview Type**: _____

Firm/Person: _____ Grower ID/Bus. Lic. No. _____

Company Type: Pest Control Business / Grower (circle one) Person Interviewed: Employer / Employee (circle one)

Pesticide(s) used:

Name of Medical Supervisor: _____

Name/Address of Medical Facility: _____

	Observations	Status*	Remarks
1.	Use records retained / 3 years [3 CCR 6728(a)].		
2.	Drs. Agreement available at the employer's location and contains all the required information / 3 years [3 CCR 6728(b)].		
3.	Drs. Agreement available at CAC's office [3 CCR 6728(b)].		
4.	Records: Items 1 & 2 plus Med. Sup recommendations & records of test dates for each employee tested / 3 years [3 CCR 6728(c)].		
5.	Medical supervision posting [3 CCR 6728(c)(5)].		
6.	Employees are informed of ChE test results (describe in remarks***).		
7.	Employer follows the recommendations made by medical supervisor 3CCR § 6728(c)(4) (describe in remarks***).		
8.	Employer investigates the work practices when employee test results are below threshold [3 CCR 6728(d)] (describe in remarks***).		
9.	Employees are removed from exposure to ChE pesticides when test results are below the threshold [3 CCR 6728(e)].		
10.			

Remarks:

*Status Indicators

C- in compliance N - not in compliance O - not observed X - not required

** Interview Type 1) HQ Inspection, 2) On-site visit (interview only), 3) Other

*** Use additional sheet(s) as necessary.

DPR 2014 Medical Supervision Survey April 17, 2014

Appendix G: REFERENCES

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