Nos. 13-17430, 14-15108

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

VIETNAM VETERANS OF AMERICA, et al.,

Plaintiffs-Appellants/Cross-Appellees,

v.

CENTRAL INTELLIGENCE AGENCY, et al.,

Defendants-Appellees/Cross-Appellants.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

REPLY BRIEF FOR DEFENDANTS-APPELLEES/CROSS-APPELLANTS

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REPLY BRIEF FOR DEFENDANTS-APPELLEES/CROSS-APPELLANTS

INTRODUCTION AND SUMMARY

The government submits this reply brief in support of its cross-appeal challenging the final judgment and injunction issued by the district court requiring the Army to develop a plan to acquire new information that may affect the well-being of former participants in chemical and biological testing programs conducted by the Army in the period from World War II to 1976, and to begin transmitting any information obtained since 2006 to class members under close and ongoing supervision by the district court.

As explained in our opening brief, the district court's "notice" injunction must be vacated because the notice provision of AR 70-25 imposes no duty on the Army to locate and provide new information to participants in testing programs conducted decades earlier, much less an unambiguous directive that is sufficiently "discrete and mandatory" to be enforceable in an action to compel agency action unlawfully withheld or delayed under 5 U.S.C. § 706(1). *See Norton v. Southern Utah Wilderness Alliance*, 542 U.S. 55, 64 (2004) (holding that "a claim under § 706(1) can proceed only where a plaintiff asserts that an agency failed to take a *discrete* agency action that it is *required to take*"). As the district court recognized, it is not clear whether AR 70-25 establishes an ongoing duty to warn "owed to individuals who participated in experiments before 1988 or whether it is limited to only those who might have done so after AR 70-25 was revised in 1988." ER 44. That conceded ambiguity in the scope and application of AR 70-25 precludes any claim that the Army violated a "duty to warn" enforceable under Section 706(1), which is limited to circumstances where "the agency's legal obligation is so clearly set forth that it could traditionally have been enforced through a writ of mandamus." *Hells Canyon Pres. Council v. U.S. Forest Serv.*, 593 F.3d 923, 932 (9th Cir. 2010).

Nowhere in their responsive brief do plaintiffs demonstrate that the notice provision of AR 70-25 imposes a clear duty on the Army, enforceable under Section 706(1), to provide additional notice to former test participants beyond the notice the Army has already provided (in conjunction with the VA) and continues to provide

through ongoing outreach efforts. Plaintiffs essentially ignore the district court's finding that the application of AR 70-25 to former test participants is not clear – a finding that singlehandedly precludes any relief under Section 706(1). Instead, plaintiffs argue that the court's broad conception of the "duty to warn" imposed by AR 70-25 was correct and that it trumps the Army's interpretation of that provision. These arguments fail at every turn.

As explained more fully below, the notice provision in AR 70-25 is silent regarding past testing programs, and there are many indications that the "duty to warn" in that provision does not apply retroactively to participants in testing programs conducted many decades earlier. The Army reasonably construes that provision to apply solely to research conducted after the effective date of AR 70-25 (February 24, 1990), and the district court identified no proper basis for ignoring the principle that an agency's interpretation of its own regulation is normally entitled to considerable deference. At a minimum, the court erred in concluding that plaintiffs' interpretation of that provision was "more persuasive," ER 50, and then transforming a contested construction of an ambiguous regulation into an unprecedented and expansive directive to provide additional notice to former test participants.

Plaintiffs likewise fail to offer any meaningful response to the argument in our opening brief that their "notice" claim is, at bottom, a prohibited challenge to the *sufficiency* of the notice and outreach the Army has already provided, and continues to provide, to former test participants. Plaintiffs do not dispute that the government has

undertaken substantial efforts to determine what adverse health effects exposure to particular substances might cause and to make relevant information available to all known test participants. Nor do they identify any new information that the Army has withheld. Indeed, plaintiffs have not demonstrated, or even argued, that there is any additional information in the Army's possession that is has failed to make available to test participants. Nevertheless, plaintiffs insist that the Army failed to provide some form of "notice" that it was required to provide under AR 70-25. But the district court made no finding that there was any new information affecting the health or well-being of former test participants that the Army failed to provide. Thus, the necessary factual predicate for compelling agency action under Section 706(1) – a finding of unreasonable delay or unlawful withholding of discrete and required agency action – is missing in this case. While the district court apparently believed that the Army should be doing more to obtain and disseminate new information that could potentially affect the well-being of former test participants, AR 70-25 does not require any action by the Army with the specificity required to be enforceable under Section 706(1), and the court lacked authority simply to order the Army to do more.

In the end, the arguments in plaintiffs' responsive brief simply underscore that the "notice" injunction is based on the district court's belief that the Army *should* be gathering and providing more information to former test participants rather than any specific requirements set forth in AR 70-25. Plaintiffs contend that the regulation imposes both discrete and non-discretionary duties on the Army to provide notice,

but they nowhere identify any language prescribing action by the Army with the degree of specificity to be enforceable under Section 706(1). Nor do plaintiffs offer any response to the arguments in our opening brief that the court's injunction goes well beyond any actions even arguably identified in AR 70-25, requiring the Army to adopt new policies and procedures for the collection and dissemination of additional information to test participants and to submit its compliance plan to the court for review and approval. ER 10-11. The district court recently rejected the initial compliance plan filed by the Army, and the regime of ongoing judicial oversight the court has established to superintend the Army's compliance with ambiguous language in one of its own regulations is, to our knowledge, unprecedented. Because the court's "notice" injunction is fundamentally incompatible with the limited authority conferred in Section 706(1), it should be vacated.

ARGUMENT

THE DISTRICT COURT ERRED IN HOLDING THAT AR 70-25 COMPELS THE PROVISION OF ADDITIONAL "NOTICE" TO CLASS MEMBERS BEYOND THE NOTICE THE ARMY AND THE VA HAVE ALREADY PROVIDED AND CONTINUE TO PROVIDE.

As explained in our opening brief (at 24-25), Section 706(1) does not confer authority on courts to "compel agency action merely because the agency is not doing something [a court] may think it should do." *Zixiang Li v. Kerry*, 710 F.3d 995, 1004 (9th Cir. 2013). Instead, judicial review under Section 706(1) is strictly limited in order "to protect agencies from undue judicial influence with their lawful discretion, and to

avoid judicial entanglement in abstract policy disagreements about which courts lack both expertise and information to solve." *SUWA*, 542 U.S. at 66. As the Supreme Court has summarized, "a claim under § 706(1) can proceed only where a plaintiff asserts than an agency failed to take a *discrete* agency action that it is *required to take*." *Id.* at 64 (emphases in the original). Moreover, as this Court has cautioned, plaintiffs may not evade the APA's final agency action requirement "with complaints about the sufficiency of agency action dressed up as an agency's failure to act." *Ecology Ctr., Inc. v. United States Forest Serv.*, 192 F.3d 922, 926 (9th Cir. 1999).

Plaintiffs do not dispute any of these legal principles in their responsive brief. They concede that courts may only compel agency action under Section 706(1) in limited circumstances where the action allegedly withheld is both "discrete" and "legally required." *Hells Canyon*, 593 F.3d at 932. Plaintiffs' sole argument on appeal is that the notice provision in the 1990 version of AR 70-25 imposes a broad duty on the Army to locate and provide new information to former participants in testing programs conducted decades earlier that is sufficiently discrete, mandatory, and unambiguous to be enforceable under Section 706(1). They are mistaken.

A. The District Court Erred In Construing The Notice Provision In The 1990 Version of AR 70-25 To Impose An Ongoing Duty To Warn Individuals Who Participated In Research Programs Completed Decades Prior To Its Effective Date.

1. Plaintiffs' claim that they are entitled to a more robust form of "notice" than the historic and ongoing notice and outreach the Army is currently providing rests

exclusively on a single provision in the 1990 version of AR 70-25, which establishes prospective requirements for obtaining the informed consent of volunteers regarding their participation in research conducted by the Army. That provision states in full:

> *b. Duty to warn.* Commanders have an obligation to ensure that research volunteers are adequately informed concerning the risks involved with their participation in research, and to provide them with any newly acquired information that may affect their well-being when that information becomes available. The duty to warn exists even after the individual volunteer has completed his or her participation in research. To accomplish this, the MACOM [major Army Commands] or agency conducting sponsoring research must establish a system which will permit the identification of volunteers who have participated in research conducted or sponsored by that command or agency, and take actions to notify volunteers of newly acquired information. (See *a* above.)

AR 70-25 § 3-2.h (Plaintiffs' Statutory Addendum 168).

On its face, the notice provision says nothing about providing retroactive notice or any sort of "warnings" to participants in Army testing programs that were completed long before the effective date of AR 70-25 (February 24, 1990). *See* Pl. Add. 150. Where regulations specify an effective date, they are normally construed not to have retroactive application, *see United States v. Gomez-Rodriguez*, 77 F.3d 1150, 1153-54 (9th Cir. 1996), and this legal presumption applies with special force where (as here) the consequences of retroactive application would be enormous. As explained in our opening brief (at 40), and by the Army's designated witness under Fed. R. Civ. P. 30(b)(6), Dr. Michael Kilpatrick, the notice provision was only intended to apply prospectively – to hypothetical *future* participants in Army testing programs. Indeed, if the Army had intended for this provision to impose a broad

duty to provide retroactive notice of possible health effects to past participants in prior Army testing programs, that provision would almost certainly have included at least some discussion of how that massive undertaking should be completed. The absence of any such discussion is telling. In short, there is not the slightest indication on the face of the notice provision in AR 70-25 that the Army intended to unilaterally commit itself to the burdensome task of collecting and disseminating new information that could potentially affect the well-being of individuals who participated in tests completed long before that regulation was promulgated.[1]

On the contrary, both the language and the context of AR 70-25 confirm that the "duty to warn" in that provision is tied exclusively to research taking place after 1990. By its plain terms, the notice provision establishes a *prospective* duty, requiring commanders "to ensure that research volunteers are adequately informed concerning the risks involved with their participation in research." Pl. Add. 168. Indeed, the final sentence in the notice provision explains that the way in which the Army will satisfy this duty is to "establish a system which will permit the identification of volunteers who have participated in research conducted or sponsored by that command or agency, and take actions to notify volunteers of newly acquired information." *Id.*

[1] Although prior versions of AR 70-25 were in effect during some part of the time that the testing programs at issue in this case were being conducted, neither the 1962 version of that regulation, Pl. Add. 16-23, nor the 1974 version, *id.* at 24-30, contains any provision imposing a "duty to warn," and the district court expressly found that these earlier versions of AR 70-25 were "directed at the provision of informed consent *prior to* participation in the experiments." ER 43 (emphasis added).

That provision concludes with a parenthetical reference to "*a* above," which is a separate provision imposing prospective obligations. *Id.* at 163-64 (AR 70-25 § 3-2.a(1)(d)) (stating that commanders "will" publish directives and regulations including "procedures to assure that the organization can accomplish its 'duty to warn.'"). In short, the plain language and overall structure of AR 70-25 confirm what the Army's designee under Rule 30(b)(6) explained in deposition testimony requested by plaintiffs: that the "duty to warn" in that regulation is "part of the informed consent process at the beginning of any research study," and that this duty cannot be "retrofit" to apply to completed research programs. CR 496, Ex. 4, at 143 (testimony of Dr. Kilpatrick). *See also id.* at 139 ("To be able to effect a duty to warn at the time a research program is being established, this process would have to be established.").[2]

In light of the forward-looking language and structure of AR 70-25, the district court conceded that there is "nothing that clearly requires that these provisions apply to those who became test volunteers before they were created." ER 44. This recognition that AR 70-25 does not "clearly" apply to former test participants should

[2] The requirement in AR 70-25 that the Army create a "volunteer data base" further confirms that the "duty to warn" applies solely to research programs conducted after the effective date of that regulation. The system of records notice (required by the Privacy Act) for the "Medical Research Volunteer Registry" developed pursuant to AR 70-25 states that it includes records of individuals "participating in current and future research." 56 Fed. Reg. 48,168, 48,187 (Sept. 24, 1991). In contrast, a separate notice published that same day stated that the system of records that would become the database for Cold War-era test participants would cover individuals "who participated in Army tests of potential chemical agents and/or antidotes from the early 1950s until the program ended in 1975." *Id.* at 48,180.

have ended the court's analysis under Section 706(1), because that provision only applies where legal obligations are so clearly set forth that they could be "enforced through a writ of mandamus." *Hells Canyon*, 593 F.3d at 932. But the district court ignored this fundamental limit on relief under Section 706(1) and performed its own analysis of AR 70-25, concluding ultimately that plaintiffs' construction of that regulation – to impose a duty "owed to service members who became test subjects before 1988" – was "more persuasive" than the Army's construction of its own regulation. ER 50. That legal error alone compels vacatur of the "notice" injunction.

2. Plaintiffs' attempts to defend the injunction fail on several levels. As an initial matter, they do not even attempt to address the district court's finding that it is not clear whether AR 70-25 applies to participants in testing programs conducted prior to 1988. AR 44. In a footnote, plaintiffs suggest that "[t]he Army overstates the court's order, which did not find that the duty was unclear." Yellow Br. 29 n.17. But plaintiffs' assertion that the district court "conducted a thorough analysis of the issue, and found in Plaintiffs' favor," *id.*, does not dispel the ambiguity the court found in that provision. On the contrary, it shows that the court engaged in an impermissible inquiry to determine what duties AR 70-25 might establish – weighing plaintiffs' construction of that provision against the Army's construction – even though Section 706(1) only permits the enforcement of unambiguous legal obligations. Plaintiffs nowhere offer any response to our argument that the court erred in undertaking an inquiry to "clarify" the duties it believed AR 70-25 imposed on the Army.

In any event, plaintiffs' contention that the district court properly construed that regulation is also unavailing. Plaintiffs ignore the many textual and structural indications discussed above indicating that the notice provision was meant to apply solely to prospective research. Instead, they focus on language in that provision indicating that it is forward-looking. *See* Yellow Br. at 26 (citing provision requiring system to provide for the "identification of volunteers *who have participated* in research") (emphasis added). But the Army has never disputed the forward-looking nature of the obligations imposed by AR 70-25. Thus, although plaintiffs are correct that the "regulation contemplates providing notice to former test subjects after their testing participation has ended," *id.*, this observation is irrelevant to the central question at issue in this case: whether that forward-looking duty applies solely to *future* testing programs conducted after the effective date of that provision or applies retroactively to all prior programs ever conducted by the Army at any time.

As outlined above, the effective date of AR 70-25, the need for systems to be established at the time research commences in order to provide effective notice to test participants, and the absence of any indication that the Army was committing itself to the enormous, new task of providing retroactive notice to all former test participants in chemical and biological testing programs conducted many decades ago all strongly suggest that AR 70-25 applies solely to future testing programs. Indeed, provisions in Appendix F to the 1988 and 1989 versions of AR 70-25 expressly exempted "[r]esearch involving deliberate exposure of human subjects to nuclear weapons

effect, to chemical warfare agents, or to biological warfare agents" from coverage under that regulation. *See* Pl. Add. 71-72 (1988); 128-29 (1989). There is thus no doubt that the notice provision in the 1988 and 1989 versions of AR 70-25 did not impose a retroactive "duty to warn" former participants in the testing programs at issue in this case. Because the language of the notice provision in the 1990 version of AR 70-25 is identical to the language in the prior versions, there is likewise no basis for construing that language to impose a broad duty to warn past test participants.

Plaintiffs' entire argument that the duty to warn in the notice provision of the 1990 version of AR 70-25 applies retroactively to all testing programs ever conducted by the Army rests solely on a modification to that regulation made in 1990, which moved the provision identified above regarding the "deliberate exposure of human subjects" to various dangerous agents from the appendix enumerating *exemptions* from the regulation's coverage to Section 1-4.d(4), a provision listing subjects *covered* by the regulation. According to plaintiffs, this new provision would be superfluous unless the notice provision of AR 70-25 is deemed to apply to the testing programs at issue in this case because the Army no longer conducts research involving the deliberate exposure of test participants to dangerous agents. Yellow Br. 26-27. The district court likewise relied heavily on this provision and invoked the canon against construing statutes and regulations to render any terms superfluous. ER 50-51. However, this modification to the overall coverage of AR 70-25 did not expand the "duty to warn" in the notice provision of the regulation, whose language did not

change. In short, the new provision in the 1990 version of AR 70-25 cannot bear the weight plaintiffs and the district court have assigned to it.

Nothing in the 1990 version of AR 70-25 suggests that the modification identified by plaintiffs was intended to have the extraordinary consequence of changing the scope and application of the notice provision. On the contrary, the "summary of change" in the preface to the 1990 version of the regulation states that it was published solely to correct a mistake made in the 1989 version of the regulation in "respond[ing] to guidance from the Office of the Judge Advocate General that a subparagraph be moved from the text of the regulation to Appendix F," because "the wrong sub-paragraph was moved." Supp. Stat. Add. (attached hereto).[3] Nowhere does the regulation suggest that any change was being made to suddenly expand the prospective duty to warn in AR 70-25 to participants in decades-old testing programs.

In any event, the provision referencing research involving the deliberate exposure of human subjects to dangerous agents in the 1990 version of AR 70-25 is

[3] Although plaintiffs reproduced what appeared to be the full text of the 1990 version of AR 70-25 in their statutory addendum, Pl. Add. 150-207, they did not include the "summary of change" that preceded that regulation, and we have therefore attached the full text of the 1990 version of that regulation as an addendum to this brief. Notably, the "summary of change" suggests that the only change that should have been made was to move a sub-paragraph from the text of the regulation to Appendix F (exemptions). Instead of simply making this change, however, sub-paragraph (h) regarding "research involving deliberate exposure of human subjects" to dangerous agents was also moved *from* Appendix F *to* the text of the regulation. In short, it appears that the migration of subsection (h) from the exemptions from coverage under AR 70-25 was simply a mistake – albeit a mistake without consequences until plaintiffs and the district court seized on it in this case.

not superfluous under the Army's construction of the notice provision. Although the Army unilaterally suspended the volunteer testing programs at issue in this case in 1976, there was no statutory bar on the resumption of such research as of 1990. The general prohibition on such testing, which still allows limited exceptions for research involving protective counter-measures against such agents, was enacted in 1997. *See* 50 U.S.C. § 1520a, Pub. L. No. 105-85, Div. A, title X, § 1078 (Nov. 1997); H. Conf. Rep. No. 105-340 (1997). Thus, in 1990, the expansion of AR 70-25 to encompass the possible resumption of *future* tests involving the deliberate exposure of individuals to dangerous agents was reasonable – not mere surplusage, as plaintiffs contend.

Finally, as explained in our opening brief (at 42), the Army still has authority to conduct research involving the use of human subjects in controlled clinical trials to evaluate the safety and effectiveness of medical products designed to *protect* against chemical agents – that is, defensive measures such as the anthrax vaccine. *See* 50 U.S.C. § 1520a (permitting tests or experiments carried out for "any purpose that is directly related to protection against toxic chemicals or biological weapons and agents"). Plaintiffs ignore this express statutory authority to conduct research related to counter-measures because it further refutes their argument that the change to the 1990 version of AR 70-25 would be rendered superfluous under the Army's interpretation of the duty to warn. Instead, they selectively cite the Army's "medical countermeasures" web site, SER 54, arguing that it conclusively establishes that the Army no longer conducts tests that fall within the coverage of the provision added to

AR 70-25 in 1990. As explained above, whether or not that provision is superfluous now is irrelevant to the question whether it was surplusage when added, but plaintiffs also err in suggesting that it is superfluous even now. Most notably, plaintiffs ignore the statement on the Army's web site, which tracks the language of 50 U.S.C. § 1520a, that the Army still conducts "medical & biological defense programs that involve the use of human subjects in controlled clinical trials to test and evaluate the safety and effectiveness of medical products (drugs, therapies, etc.) to protect against chemical agents," and that "[t]he use of human subjects in these trials involves volunteers who have provided informed consent." SER 54.

In sum, plaintiff err in arguing that a technical amendment to the 1990 version of AR 70-25 (which appears to have been a mistake) would be rendered superfluous unless their broad conception of the "duty to warn" is accepted.

B. The District Court Erred In Rejecting The Army's Reasonable Construction Of Its Own Regulation.

Even if plaintiffs' broad construction of AR 70-25 were plausible, it does not trump the Army's reasonable construction of its own regulation, much less do so with sufficient clarity to create duties enforceable under Section 706(1). Plaintiffs argue at length that the Army's interpretation of AR 70-25 is not entitled to any deference, Yellow Br. 28-32, but they do not identify any proper basis for disregarding the considered judgment of the agency that promulgated that regulation. In any event, the ultimate question is not, as the district court framed it, whether plaintiffs'

interpretation "is more persuasive" than the Army's, ER 50, but whether in light of the ambiguity in that regulation, it imposes a duty enforceable under Section 706(1).

Plaintiffs do not dispute the basic rule that an agency's interpretation of its own regulation is normally entitled to considerable deference. *See Auer v. Robbins*, 519 U.S. 452 (1997). They argue instead that two exceptions to that rule are applicable here: (1) where the agency's interpretation is a "post hoc rationalization," and (2) where the regulation is unambiguous. *See* Yellow Br. at 28-29. Neither of these exceptions applies in this case.

As explained above, and in our opening brief, AR 70-25 is, at a minimum, ambiguous, and in such circumstances an agency's construction of its own regulation controls, so long as it is reasonable. *See Lezama-Garcia v. Holder*, 666 F.3d 518, 525 (9th Cir. 2010). The district court conceded that it was not clear whether AR 70-25 creates an ongoing "duty to warn" with respect to participants in testing programs prior to 1988, *see* ER 44, and plaintiffs' unsupported assertion that "AR 70-25 is not" ambiguous, Yellow Br. 29, cannot be squared with the court's finding. Indeed, plaintiffs advance no argument whatsoever to support their claim that the regulation is not ambiguous. They simply make this remarkable assertion and then proceed to argue that "even agency interpretations of ambiguous regulations are not entitled to deference if there is 'reason to suspect that the interpretation does not reflect the agency's fair and considered judgment on the matter in question.'" *Id.* (citing *Auer*, 519 U.S. at 461). This legal principle does not advance plaintiffs' case.

Plaintiffs do not identify any reason to believe that the Army's construction of AR 70-25 "does not reflect the agency's fair and considered judgment." Most notably, plaintiffs do not cite any prior interpretation of AR 70-25 contrary to the one propounded by the Army in this case. Plaintiffs emphasize "that the Army's interpretation of AR 70-25 was offered for the first time this litigation," Yellow Br. 30, but that alone is not cause for skepticism or suspicion, particularly in the context of an action under Section 706(1). As explained in our opening brief (at 41), this Court has long recognized that the "post hoc rationalization" rule does not apply in Section 706(1) cases, where "there is no official statement of the agency's policy and relevant justifications." *Independence Mining Co. v. Babbitt*, 105 F.3d 502, 511–12 (9th Cir. 1997). Although plaintiffs attempt to distinguish *Independence Mining* on the ground that it does not *require* deference to an agency's construction of a regulation in the context of litigation, Yellow Br. 31, that decision plainly stands for the proposition that agency interpretations in the course of litigation under Section 706(1) are not suspect simply because they are advanced for the first time in litigation. *Cf. Chase Bank USA, N.A. v. McCoy*, 131 S. Ct. 871, 880–81 (2011); *Talk America, Inc. v. Michigan Bell Tel. Co.*, 131 S. Ct. 2254, 2263-64 (2011).

Plaintiffs suggest that the district court was entitled to disregard the Army's construction of AR 70-25 simply because the court disagreed with the testimony of the Army's designee under Fed. R. Civ. P. 30(b)(6). But the district court did not identify any serious errors in the testimony of the Army's witness, and the court itself

erred in concluding that Dr. Kilpatrick "was mistaken about the date on which the operative parts of the regulation were amended, suggesting that he did not have a clear understanding of the context in which these changes were made." ER 48. The court did not identify any specific testimony by Dr. Kilpatrick that was supposedly erroneous, and the court's citation to the 1988 version of AR 70-25, *see* ER 48, an earlier version of the regulation that no one contends applies here, strongly suggests that the court (not Dr. Kilpatrick) was confused about the applicable regulations.[4] Likewise, the court's statement that the Army's position was "developed quickly and without full consideration of AR 70-25," ER 48, ignores the unique context in which this issue was presented. Plaintiffs obtained testimony from a government witness on this issue under Rule 30(b)(6), over the Army's objections, and the district court could not ignore that testimony simply because the court disagreed with it on the merits.

[4] In a similar vein, the district court declared that the testimony of the Army's Rule 30(b)(6) witness with respect to the need to create databases containing test participants at the *beginning* of research studies "is simply not accurate." ER 48. Here again, however, the court's apparent disagreement with the government's witness rests on an erroneous assumption by the court: that sufficient information will be available after the fact to create a database compliant with AR 70-25. Indeed, one of the central premises of plaintiffs' claim in this case is that the World II and Cold War-era databases created by the Army and the VA after the fact are *not* sufficient to satisfy the putative duty to warn in AR 70-25 because they do not contain enough information to notify all test participants. It is undisputed that the decades-old testing programs at issue in this case were not designed to track long-term health outcomes and thus had less extensive recordkeeping than they would today. However, this fact simply underscores that AR 70-25 was not intended to extend a "duty to warn" to testing programs that ended before the effective date of that regulation.

In sum, plaintiffs have not identified any legitimate bases on which the district court could properly have disregarded the Army's reasonable construction of AR 70-25. Until this litigation, no court ever had occasion to construe that regulation, and no one – including Congress, the Army, or even plaintiffs – had ever previously suggested that AR 70-25 imposes expansive "notice" obligations on the Army of the sort the district court has now divined. Indeed, as noted in our opening brief (at 41 n.10), the lead plaintiff in this case, the Vietnam Veterans of America, issued advisory notices to its members prior to this case explaining that the VA, not the Army, has a duty to provide notice to test participants. SER 46, 51. Plaintiffs' pre-litigation views are entirely consistent with the "Bob Stump Act," in which Congress required the Secretary of Defense to work with veterans and veterans service organizations to identify – not notify – test participants. *See* National Defense Authorization Act for Fiscal Year 2003, Pub. L. No. 107-314, Div. A., Title VII, Subtitle A, § 709(c), 116 Stat. 2458, 2587 (2002). Plaintiffs nowhere dispute these points, and they further demonstrate that the Army's reasonable construction of AR 70-25 is not only correct but also entitled to considerable deference.

C. The District Court Erred In Allowing Plaintiffs To Challenge The Sufficiency Of The Army's Ongoing Notification And Outreach Efforts To Former Test Participants.

As explained in our opening brief (at 43-44), although the district court purported to recognize the principle that suits may not proceed under Section 706(1) where they challenge the *sufficiency* of agency action, *see Ecology Ctr.*, 192 F.3d at 926,

the court allowed just such a challenge to the Army's ongoing notification and outreach efforts. The court expressly acknowledged the substantial efforts the Army (in conjunction with the VA) has undertaken to determine what adverse health effects exposure to particular substances might cause and to make all relevant information available to former test participants, and the court made no finding that there was any new information in the Army's possession that it has unlawfully withheld. Nevertheless, the court concluded that the Army has an ongoing duty to warn, and found that plaintiffs could "properly attack the Army's failure to act" because the Army had not presented any evidence that it "sent any updated information to test subjects" since 2006 and had "not acknowledge[d] any intent or duty to do so." ER 54. In this way, the court allowed a claim for additional notice beyond what the Army is already providing and did so without making the requisite predicate finding necessary to compel agency action under Section 706(1): that the Army failed to provide specific new information that it was legally required to provide.

Plaintiffs' response to these arguments underscores the degree to which the district court's injunction addresses the *sufficiency* of the Army's overall notification and outreach efforts rather than the Army's *failure* to take any discrete and mandatory action required by AR 70-25. Plaintiffs do not dispute that the Army has provided information to former test participants in the form it believes is most appropriate and continues to make relevant information available to veterans in a variety of different ways, including the operation of a public website for veterans which contains, among

other things, long-term studies concerning testing programs and identifies a 1-800 number allowing veterans to obtain their service member test files containing the information DoD has about various tests. Yet plaintiffs repeatedly contend that these "passive activities are not the notice required by the regulation." Yellow Br. 40. Indeed, plaintiffs directly challenge the Army's ongoing notification and outreach efforts, expressing outrage that the "Army would apparently require that a Test Subject Veteran know that he must affirmatively contact the Army, and continuously check the website or repeatedly call the 1-800 number in hopes of obtaining any new information." *Id.* at 41. In this way, plaintiffs' own arguments undermine any plausible contention that their "notice claim is not for 'additional notice.'" *Id.* at 39.

Plaintiffs' response to the argument that the district court made no proper finding that the Army failed to take any action that it was legally required to take, *see SUWA*, 542 U.S. at 64, is similarly flawed. Plaintiffs make no effort to identify any significant new information regarding possible effects on the health and well-being of test participants that the Army has not disclosed, or even to suggest any categories of information that might exist.[5] Instead, they insist that the district court made the necessary predicate finding that the Army failed to act when it concluded that the

[5] As explained in the Army's April 16, 2014 supplemental compliance plan, which the district court ordered the Army to file in its April 2, 2014 order deeming the Army's initial report insufficient, the Army has no new information concerning long-term health effects that may affect the well-being of former test participants that has not already been made available to them. *See* CR 563, at 3 (citing declarations).

Army has "not provided evidence that they have sent any updated information to test subjects since the DVA sent the notice and letters and do[es] not acknowledge any intent or duty to do so." Yellow Br. 38 (citing ER 54). Moreover, plaintiffs contend that this is a factual finding reviewed solely for "clear error." *Id.*

This gets matters precisely backward. Plaintiffs had the burden to establish a failure to act under Section 706(1), and they failed to satisfy that burden because they failed to show – and the district court failed to find – that there was any new information available to the Army that it had a discrete and mandatory duty to provide to veterans. In the absence of any such finding, the district court could not properly draw the legal conclusion that the Army failed to act within the meaning of Section 706(1). In short, the court made no factual finding insulated from appellate review under a clear error standard; it simply concluded that the Army had not provided additional notice to veterans in ways other than through its public website, its 1-800 number and its responses to requests from individual veterans for their test files. Thus, the court not only failed to make the necessary predicate finding to establish a violation of Section 706(1), it also improperly evaluated the sufficiency of the Army's current notification and outreach efforts in concluding that the Army had not done enough to notify former test participants.

D. The District Court Erred In Issuing An Injunction That Establishes A Regime Of Judicial Oversight To Compel Action By The Army Far Beyond Any Discrete And Mandatory Duties Identified In The Notice Provision Of AR 70-25.

Apart from the district court's erroneous construction of AR 70-25, its failure to properly defer to the Army's reasonable construction of that regulation, and its impermissible assessment of the sufficiency of the Army's ongoing notification and outreach efforts, the court independently erred in issuing a broad injunction exercising ongoing oversight and control over the Army untethered from any discrete and mandatory duties identified in AR 70-25.

As explained in our opening brief (at 42-43), whatever duty to warn AR 70-25 might be thought to impose is inherently unsuitable for enforcement under Section 706(1) because the scope of any "notice" to be provided will inevitably turn on a host of discretionary scientific judgments about what constitutes new information that "may affect" the well-being of former test participants and policy judgments about what information is significant enough to warrant sending new notices to veterans that may unnecessarily alarm them. *See* SER 8-9 (Decl. of Dee Dodson Morris ¶ 19); *In re Consol. U.S. Atmospheric Testing Litig.*, 820 F.2d 982 (9th Cir. 1987) (recognizing discretionary nature of "duty to warn" in context of FTCA claim). Indeed, the discretionary and inherently malleable nature of the "duty to warn" is reflected in the court's injunction, which does not specifically direct the provision of any particular form of notice to any particular class members but instead orders the Army to come

up with plans "in its discretion" for gathering information that could affect the well-being of test participants and for transmitting such information. ER 11.

On appeal, plaintiffs contend that the broad way in which the injunction is framed adequately preserves the Army's discretion to gather information and provide notice in whatever ways it deems fit and thus does not impermissibly trench on the agency's discretion in carrying out its duties. Yellow Br. 35 (arguing that the district court properly "compel[ed] the Army to comply with its duty to warn without directing how it must do so"). In reality, however, the injunction imposes a variety of burdensome, new programmatic requirements to develop plans to perform enormous and ill-defined searches and data-gathering tasks and, if relevant information is obtained, to synthesize and evaluate that information for possible dissemination to subsets of former test participants. Moreover, the injunction rejects the course of action the Army has thus far undertaken and imposes a regime of ongoing judicial oversight to enforce nebulous standards. This result is far more intrusive than a discrete court order to do a specific thing by a specific date.

A recent order issued by the district court underscores the degree to which the broad "notice" injunction will improperly embroil the court in the micro-management of the Army's notification efforts. On April 2, 2014, notwithstanding the language in the court's injunction purporting to allow the Army considerable discretion in formulating plans to provide additional notice to class members, ER 11, the court largely rejected the compliance plan filed by the Army, finding that the agency's

proposed plan for gathering new information "is unduly time-consuming and vague." CR 562, at 2. Without any reference to any discrete duty contained in AR 70-25, the court directed the Army to file a new plan within 14 days, specifying that it "must include an actual timeline for completion of the search for Newly-Acquired Information" and "identify the job titles" of Army leaders charged with responsibility for locating new information. *Id.* at 3. In short, the district court is not merely ordering the Army to perform discrete tasks specified in statutes or regulations; it is undertaking the sort of programmatic oversight precluded under Section 706(1).

In sum, the district court's retention of jurisdiction to indefinitely monitor compliance with its injunction is fundamentally at odds with the limited authority conferred by Section 706(1) to compel discrete and mandatory action that has been unlawfully withheld or unreasonably delayed. Plaintiffs cite no cases in which courts have exercised continuing oversight over the government's performance of analogous actions under Section 706(1), and the government is not aware of any such decisions. Plaintiffs cite two cases for the uncontroversial proposition that district courts retain jurisdiction to enforce the terms of injunctions they have issued, *see* Yellow Br. at 27-28 (citing *Sierra Club v. Penfold*, 857 F.2d 1307 (9th Cir. 1988), and *United States v. Fisher*, 864 F.2d 434 (7th Cir. 1988)), but neither case involved a claim under Section 706(1), much less involved the sort of open-ended and indefinite judicial oversight the district court is exercising here. As the court's most recent order rejecting the Army's compliance plan reflects, the district court's "notice" injunction goes far beyond any

discrete and mandatory actions even arguably identified in AR 70-25, and it is thus wholly inconsistent with the limited scope of judicial authority conferred under Section 706(1). *See SUWA*, 542 U.S. at 66 (stating that judicial review to compel agency action is carefully circumscribed "to protect agencies from undue judicial influence with their lawful discretion, and to avoid judicial entanglement in abstract policy disagreement which courts lack both expertise and information to solve").

CONCLUSION

For the foregoing reasons, and those stated in our opening brief, the district court's decision holding that the Army has a duty enforceable under 5 U.S.C. § 706(1) to provide additional notice of possible adverse health effects from past testing programs should be reversed, and the court's permanent injunction directing the Army to provide such notice should be vacated.

Respectfully submitted,

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APRIL 2014

CERTIFICATE OF COMPLIANCE

I hereby certify that this brief complies with the requirements of Fed. R. App. P. 32(a)(5) and (6) because it has been prepared in 14-point Garamond, a proportionally spaced font. I further certify that this brief complies with the type-volume limitation set forth in Fed. R. App. P. 32(a)(7)(B) because it contains 6,954 words, excluding exempt material, according to the count of Microsoft Word.

s/ Charles W. Scarborough
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CERTIFICATE OF SERVICE

I hereby certify that on April 21, 2014, I electronically filed the foregoing brief with the Clerk of Court for the United States Court of Appeals for the Ninth Circuit by using the appellate CM/ECF system.

All participants in the case are registered CM/ECF users, and service will be accomplished by the appellate CM/ECF system.

s/ Charles W. Scarborough
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STATUTORY ADDENDUM

Army Regulation 70-25 (1990)

Army Regulation 70–25

Research and Development

Use of Volunteers as Subjects of Research

Headquarters
Department of the Army
Washington, DC
25 January 1990

UNCLASSIFIED

SUMMARY of CHANGE

AR 70-25
Use of Volunteers as Subjects of Research

This change is published to correct a serious error that occurred during the final editing of the current revision. In attempting to respond to guidance from the Office of The Judge Advocate General that a subparagraph be moved from the text of the regulation to appendix F, the wrong sub-paragraph was moved.

Headquarters
Department of the Army
Washington, DC
25 January 1990

*Army Regulation 70–25

Effective 24 February 1990

Research and Development

Use of Volunteers as Subjects of Research

By Order of the Secretary of the Army:
CARL E. VUONO
General, United States Army
Chief of Staff
Official:

MILTON H. HAMILTON
Administrative Assistant to the Secretary of the Army

History. This publication was last revised on 8 August 1988. Since that time, permanent Change 1 has been issued. As of 25 January 1990, that change remains in effect. This UPDATE printing incorporates that change into the text. This UPDATE printing publishes a Change 2. The portions being revised by this change are highlighted.

Summary. This revision implements Department of Defense (DOD)Directive (DODD) 3216.2. It reflects the present legal requirements pertaining to the use of humans as research subjects funded by research, development, test, and evaluation appropriations. This revision provides guidance for establishing human use committees (HUCs). Excluding limited situations, authority to approve research using human subjects can be delegated within the military chain of command.

Applicability. This regulation applies to research, development, test, and evaluation (RDTE) programs conducted by the Active Army. It does not apply to the Army National Guard (ARNG) or the U.S. Army Reserve (USAR) unless there is involvement of Active Army personnel.

Army management control process. This regulation is subject to the requirements of AR 11–2. It contains internal control provisions but does not contain checklists for conducting internal control reviews. A checklist will be published at a later date.

Supplementation. Supplementation of this regulation is prohibited unless prior approval is obtained from HQDA (DASG–RDZ), 5109 Leesburg Pike, Falls Church, VA 22041–3258.

Interim changes. Interim changes to this regulation are not official unless they are authenticated by the Administrative Assistant to the Secretary of the Army. Users will destroy interim changes on their expiration dates unless sooner superseded or rescinded.

Suggested Improvements. The proponent of this regulation is the Office of The Surgeon General. Users are invited to send comments and suggested improvements on DA Form 2028 (Recommended Changes to Publications and Blank Forms) directly to Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

Distribution. Distribution of this publication is made in accordance with the requirements on DA Form 12–09–E, block number 3724, intended for command level D for Active Army and None for the ARNG and USAR.

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Glossary

*This regulation supersedes AR 70–25, 25 September 1989.

RESERVED

Chapter 1
Introduction

1–1. Purpose
This regulation—

a. Prescribes Army policy on the conduct and management of human subjects in testing, including—

(1) Command responsibilities.

(2) Review process requirements.

(3) Approval authorities.

(4) Reporting requirements.

b. Allows a decentralized approval option for those elements that have established review committees and an internal review process.

1–2. References
Required and related publications and prescribed and referenced forms are listed in appendix A.

1–3. Explanation of abbreviations and terms
Abbreviations and special terms used in this regulation are explained in the glossary.

1–4. Limitations
a. Nothing in this regulation is intended to supersede requirements for health hazard or other safety review required by Department of the Army(DA) regulations.

b. Nothing in this regulation limits the authority of a health care practitioner to provide emergency care under laws that apply in the jurisdiction in which care is provided.

c. Protocols for the use of drugs or Schedule I controlled substances for investigational purposes will be approved as per AR 40–7.

d. The guidance in this regulation pertains to the following, regardless of whether conducted by DA, a contractor, grantee, or other agency utilizing Army funds:

(1) Biomedical research and behavioral studies involving human subjects.

(2) RDTE involving new drugs, vaccines, biologicals, or investigational medical devices.

(3) Inclusion of human subjects, whether as the direct object of research or as the indirect object of research involving more than minimal risk in the development and testing of military weapon systems, vehicles, aircraft, and other materiel. The determination of whether a research protocol involves more than minimal risk will be made by review committees established in accordance with paragraph 3–2*b* of this regulation.

(4) Research involving deliberate exposure of human subjects to nuclear weapons effect, to chemical warfare agents, or to biological warfare agents.

(5) Activities funded by non-Army resources in which the human subjects are DA military or civilian personnel.

e. See appendix F for a listing of research exempt from the requirements of this regulation.

Chapter 2
Responsibilities

2–1. The Under Secretary of Defense for Aquisition (USD (A))
In accordance with DOD Directive 3216.2, the USD (A) or designee will be the approval authority for studies involving the actual exposure of human subjects to nuclear weapons effect, chemical warfare agents, or biological warfare agents.

2–2. Assistant Secretary of Defense (Health Affairs) (ASD (HA))
In accordance with DOD Directive 3216.2, the ASD (HA) serves as the DOD representative on matters relating to implementation of Food and Drug Administration (FDA) regulatory requirements.

2–3. Assistant Secretary of the Army (Research, Development, and Aquisition) (ASA (RDA))
The ASA (RDA) will manage all DA RDTE activities, including those in which human use is planned.

2–4. The Deputy Chief of Staff for Personnel (DCSPER)
The DCSPER will—

a. Supervise and review RDTE activities under the Army Personnel Performance and Training Program.

b. Within established areas of responsibility, monitor RDTE involving human subjects to ensure implementation of policies contained in this regulation.

c. Approve or disapprove those studies involving alcohol and drug abuse programs.

2–5. The Surgeon General
The Surgeon General (TSG) will—

a. Prepare policies and regulations on research using human subjects.

b. Establish and maintain the Human Subjects Research Review Board(HSRRB), chaired by the Assistant Surgeon General for Research and Development.

c. Establish and maintain the Human Use Review and Regulatory Affairs Office (HURRAO) attached to the U.S. Army Medical Research and Development Command (USAMRDC) and reporting to the Assistant Surgeon General for Research and Development.

d. Approve or disapprove research proposals from major Army Commands (MACOMs) that do not have a HUC or an internal review process.

e. Provide an evaluation of protocols as described in paragraphs 2–1 and 2–4, above, and 2–6, below, to the following heads of offices or command:

(1) The USD (A).

(2) The DCSPER.

(3) Upon request, the Commander, SSC–NCR.

f. Be the approval authority for studies and research protocols involving human subjects using Schedule 1 controlled drug substances.

g. Be the approval authority for research involving minors, or other vulnerable categories of human subjects, when subjects are wards of a State or other agency, institution, or entity.

h. Be the approval authority for MACOM or agency requests to establish a HUC and a human use review process.

i. Manage the Army's Health Hazard Assessment Program and assess health hazards of medical and nonmedical materiel.

j. Direct medical followup, when appropriate, on research subjects to ensure that any long-range problems are detected and treated.

k. Report on a frequent basis, findings associated with classified investigational drug and device studies to the USD (A), the ASD (HA), and the FDA.

l. Be the approval authority for all in-house and contract research(other than that noted in paras 2–1, 2–2, 2–4, and 2–6) involving human subjects for which the Army has been designated the executive agent. Except for those categories of research noted above for which TSG is specifically designated as the approval authority, the authority to approve such research may be delegated by TSG within the military chain of command to the lowest level operating a human-subjects review process approved pursuant to paragraph 3–2*b*.

2–6. Commander, Soldier Support Center—National Capital Region (SSC–NCR)
The Commander, SSC–NCR, will be the approval authority in accordance with AR 600–46 for attitude and opinion surveys or Army occupational surveys.

2–7. Major Army commanders

These commanders will—

a. Monitor RDTE involving personnel within their command to ensure effective implementation of the policies and procedures contained in this regulation.

b. Provide assistance to volunteer recruiting teams.

c. Ensure that only individuals who freely volunteer to participate are enrolled in research protocols or studies.

2–8. Commanders of RDTE organizations

These commanders will—

a. Ensure the effective implementation of the policies and procedures contained in this regulation.

b. Use the established review process through TSG's HSRRB for all protocols and test plans or establish a HUC and implement review process consistent with the policies and procedures contained in this regulation.

c. Ensure that research volunteers are adequately informed concerning the risks associated with their participation, and provide them with any newly acquired information that may affect their well-being when that information becomes available.

d. Comply with AR 40–10, AR 70–10, AR 385–16, AR 602–1, and AR 602–2 in planning and conducting development and/or operational testing.

2–9. Other responsibilities

a. Members of the HSRRB will—

(1) Evaluate methods by which DA involves human subjects in research.

(2) Recommend policy to TSG on the treatment of volunteers consistent with current moral, ethical, and legal standards. (See app G for legal implications.)

(3) Evaluate research protocols and test plans submitted to TSG for approval.

b. The Chief of the HURRAO will—

(1) Provide, for TSG, administrative support for the HSRRB.

(2) Conduct a compliance review of all protocols submitted to TSG for approval.

(3) Submit DA-sponsored Notices of Claimed Investigational Exemption for a New Drug (INDs) and Investigational Device Exemptions (IDEs) directly to the FDA.

(4) Submit DA-sponsored New Drug Applications (NDAs) directly to the FDA.

(5) Maintain DA record files for IND and NDA submissions to the FDA.

(6) Conduct post-marketing surveillance for NDAs sponsored by DA.

(7) Serve as the DA point of contact for policies and regulations on human use in RDTE programs.

(8) Advise and assist MACOMs and DA staff agencies that conduct research or sponsor research by contracts and grants that involve the use of human volunteers.

c. Investigators will—

(1) Prepare a protocol following the policies and procedures in this regulation.

(2) Prepare adequate records on—

(a) Receipt, storage, use, and disposition of all investigational drugs, devices, controlled drug substances, and ethyl alcohol.

(b) Case histories that record all observations and other data important to the study.

(c) Volunteer informed consent documents (see app E). The principal investigator will fill in the information in parts A and B of DA Form 5303–R and inform the subject of each entry on the form.

(3) Prepare progress reports, including annual reports, as determined by the approving authority and regulatory agencies.

(4) Promptly notify the approving authority, through the medical monitor, and the HUC of adverse effects caused by the research.

(5) Report serious and/or unexpected adverse experiences involving the use of an investigational device or drug to the sponsor and the FDA in accordance with AR 40–7.

(6) Ensure that the research has been approved by the proper review committee(s) before starting, changing, or extending the study.

(7) Ensure that all subjects, including those used as controls, or their representatives are fully informed of the nature of the research to include potential risks to the subject.

(8) Ensure that investigational drugs or devices are administered only to subjects under their personal supervision, or that of a previously approved associate investigator.

(9) Ensure that a new principal investigator (PI) is appointed if the previously appointed PI cannot complete the research (for example, permanent change of station (PCS), retirement, etc.).

(10) Apprise the HUC of any investigator's noncompliance with the research protocol.

(11) Seek HUC approval for other investigators to participate in the research.

(12) Ensure that research involving attitude or opinion surveys are approved in accordance with AR 600–46 (3–2*c*(5) below).

d. Volunteer recruiting teams. Members will—

(1) Establish volunteer requirements prior to recruitment.

(2) Coordinate recruiting activities with unit commanders.

(3) Undertake recruiting in a moral, ethical, and legal manner.

e. Medical monitor. The medical monitor is responsible for serving as advocate for the medical safety of volunteers. The monitor will have responsibilities as determined by the approving official and the authority to suspend or terminate the effort consistent with the policies and procedures contained in this regulation.

Chapter 3
Research

3–1. General guidance

a. Only persons who are fully informed and volunteer in advance to take part may be used as subjects in research;except, when the measures used are intended to be beneficial to the subject, and informed consent is obtained in advance from a legal representative on the subject's behalf.

b. Nothing in this regulation is intended to limit the authority of a health care practitioner to provide emergency medical care under applicable law of the jurisdiction in which care is provided.

c. Any human tissue or body fluid, obtained by autopsy, and used in research will be donated for such purpose. The donor will be the next of kin or legal representative of such person.Donation is made by written consent and relinquishes ownership and/or rights to the tissue or fluid. Consent to donate will not preclude payment for such donation. Organ donation intended for transplant will be accomplished in accordance with AR 40–3, chapter 18.

d. Any tissue or body fluid linked by identifiers to a particular person, obtained by surgical or diagnostic procedure and intended for use in research will be donated for such purpose.The donor will be the person from whom the tissue or fluid is removed or, in the event of death or legal disability of that person, the next of kin or legal representative of such person.Donation is made by written consent and relinquishes ownership and/or rights to the tissue or fluid. Consent to donate does not preclude payment for such donation.

e. The determination of level of risk in a research protocol will be made by a HUC established in accordance with this regulation.(See app G for a complete listing of legal implications.)

f. Moral, ethical, and legal concepts on the use of human subjects will be followed as outlined in this regulation. Voluntary consent of the human subject is essential. Military personnel are not subject to punishment under the Uniform Code of Military Justice for choosing not to take part as human subjects. Further, no administrative sanctions will be taken against military or civilian personnel for choosing not to participate as human subjects.

g. RDTE using human subjects is conducted in such a manner that risks to the subjects are minimized and reasonable in relation to anticipated benefits.

h. The proposed number of subjects is the minimum needed to ensure a statistically valid conclusion.

i. The research is conducted in such a manner as to avoid unnecessary physical and mental suffering. Preparations are made and adequate facilities provided to protect the subject and investigators against all foreseeable injuries, disabilities or death. Such research is not to be conducted if any reason exists to believe that death or injury will result.

j. Volunteers are given adequate time to review and understand all information before agreeing to take part in a study.

k. Volunteers are authorized all necessary medical care for injury or disease that is a proximate result of their participation in research.

(1) Medical care for civilian employees who volunteer and who perform duty as a volunteer during their regularly scheduled tour of duty will be provided in accordance with AR 40–3.

(2) Medical care costs for all other categories of personnel, who under the provisions of AR 40–3 are routinely authorized care in a military MTF will be waived for the volunteer while in the hospital, if the volunteer would not normally enter the hospital for treatment but is requested to do so to facilitate the research. This also applies to a volunteer's extension of time in a hospital for research when the volunteer is already in the hospital.

(3) Subsistence charges for all other categories of personnel, except for active duty and retired commissioned officers, may be waived in the circumstances noted in (2) above. The costs for subsistence charges for commissioned officers may be reimbursed to the officer by the research organization.

(4) Costs of medical insurance coverage or direct charges for medical care for volunteers participating in research performed by a contract or grant may be negotiated between the DA contracting officer and the contractor or grantee. (See app G.)

l. Information obtained during, or as a result of, an epidemiologic-assessment interview with a human immunodeficiency virus(HIV) serum positive member of the Armed Forces may not be used to support any adverse personnel action against the member. (See glossary for definition of the terms "epidemiologic-assessment interview," "serum positive member of the Armed Forces,"and "adverse personnel action.")

m. Research may be conducted outside the United States that involves non-U.S. citizens (for example, research on diseases of military interest, such as malaria, that are not endemic to the United States). However, in the conduct of such research, the laws, customs and practices of the country in which the research is conducted or those required by this regulation, whichever are more stringent, will take precedence. The research must meet the same standards of ethics and safety that apply to research conducted within the United States involving U.S. citizens, and will be conducted in accordance with applicable international agreements.

n. The use of prisoners of war and detainees as human research subjects is prohibited.

o. Minors may be enrolled as human research subjects when the following conditions are met:

(1) The research is intended to benefit the subject, and any risk involved is justified by the expected benefit to the minor.

(2) The expected benefits are at least as favorable to the minor as those presented by available alternatives.

(3) A legally authorized representative has been fully informed and voluntarily consents, in advance, for the minor to participate in the research.

(4) The minor, if capable, has assented in writing.In determining whether the minor is capable of assenting, the HUC will consider the minor's age, maturity, and psychological state. The HUC may waive assent for some or all minors involved in the study if it determines that the—

(a) Capability of some or all of the minors is so limited that they cannot be reasonably consulted, or

(b) Procedure involved in the research holds out a prospect for direct benefit that is important to the health or well-being of the minor, and is available only in the context of research.

p. The personnel responsible for the conduct of the research are the best qualified to recruit volunteers for a study and should be the primary recruiters whenever possible.

q. Only persons judged qualified by the appropriate approving official will conduct research involving human subjects.

r. A medical monitor is appointed by name if the HUC or approving official determines that the risk is more than minimal. A medical monitor may be appointed to minimal risk or less than minimal risk studies if so determined by the HUC or approving authority. The principal investigator may function as medical monitor only in situations where no other physician is reasonably available and approval for the principal investigator to function as medical monitor is granted by TSG. Requests for the principal investigator to function as the medical monitor will be sent to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

s. Safeguards or special conditions imposed on a protocol by a HUC may not be reduced or waived by the approving official upon approval of the protocol. The approving official may require additional safeguards, may disapprove the protocol, or may refer it to a higher review and approving authority.

t. User testing, as defined in AR 71–3, which involves the use of volunteers, is reviewed and approved by a HUC established in accordance with this regulation.

u. Research on medical devices is conducted in accordance with Part 812, Title 21, Code of Federal Regulations (21 CFR 812)

v. Emergency one-time use of an investigational drug or medical device is accomplished to the extent permitted under applicable law and in accordance with AR 40–7.

w. Public Affairs guidelines on the release of information are in AR 360–5.

3–2. Procedural guidance

a. Duties. MACOM commanders and organization heads conducting RDTE research involving human subjects will—

(1) Publish directives and regulations for—

(a) Protocol and/or test plan preparation (see app B).

(b) The use of volunteers as subjects of research conducted or sponsored by the organization.

(c) The procedures for reporting and responding to reports of improper use of volunteers as subjects of research conducted or sponsored by the organization.

(d) The procedures to assure that the organization can accomplish its "duty to warn" (see para 3–2*h* for a discussion of "duty to warn").

(2) Forward one copy of published regulations and directives(see (1) above) to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012, within 60 days of publication.

(3) Establish a HUC, if appropriate (see *b*below).

(4) Establish a system that permits the identification of volunteers who have participated in research conducted or sponsored by that command or organization. Such a system will be established in accordance with AR 340–21. (App H describes data elements which could comprise such a system.)

b. Establishing a HUC. As noted in paragraph 2–8*b*, commanders or heads of RDTE organizations will either use TSG's HSRRB or implement their own HUC.

(1) HUCs will be established for research conducted by DA in accordance with appendix C.

(2) Institutional review boards will be established by contractors or grantees in accordance with 45 CFR 46.

(3) RDTE organizations which establish an internal review process will forward the items listed below to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

(a) See *a*(2) above.

(b) A listing of the membership of the HUC and the curriculum vitae for each member.

(4) Newly established HUCs may not review research protocols until the items in *(a)* and *(b)* above are reviewed and approved by TSG.

c. Protocol and/or test plan review before submission to a HUC.

(1) A protocol or test plan will be prepared for all research requiring approval pursuant to this regulation. Certain studies may be exempt(see app F). The format in appendix B should be followed, but may be modified to meet local requirements. DA Pam 70–21 and DA Pam 71–3 provide guidance for preparation of test plans and equivalent documents. Protocols and test plans are exempt from management information requirements per AR 335–15, para 5–2*b*. An informed consent document will be prepared using DA Form 5303–R (Volunteer Agreement Affidavit), or functional equivalent, in accordance with appendix E (see *d*below). DA Form 5303–R will be reproduced locally on 8½- by 11-inch paper. A copy for reproduction is located at the back of this regulation.

(2) If a study calls for the use of tissue or fluids obtained from a human, and is not an exempt study as defined by appendix F, paragraph *e*, then a protocol is prepared.The following must be considered in determining whether informed consent is required.

(a) Fluid or tissue obtained at autopsy: informed consent is required.

(b) Fluid or tissue obtained at surgery or as the result of a diagnostic procedure and linked by identifiers directly or indirectly to a particular person intended for research: informed consent is required.

(c) Fluid or tissue obtained at surgery or as the result of a diagnostic procedure not intended for research and not linked by identifiers: no informed consent is required.

(d) Fluid or tissue obtained from a tissue or blood bank which is linked to a personal identifier and the research data is recorded in such a manner as to identify the donor: informed consent is required.

(e) Fluid or tissue obtained from a tissue or blood bank, which is linked to a personal identifier, but the research data is recorded in such a manner that the donor's identity is unknown: no informed consent is required.

(f) Fluid or tissue obtained from a tissue or blood bank which is not linked to a personal identifier: no informed consent is required.

Note. (The informed consent document used in these cases may be the DA Form 5303–R, an overprinted consent for surgery or autopsy, or other form approved by the HUC and the forms management office at the organization.)

(3) The protocol or test plan is submitted to a scientific review committee composed of individuals qualified by training and experience, and appointed by the commander of the unit to evaluate the validity of the protocol. The purpose of this peer review is to assure that the protocol design will yield scientifically useful data which meets the objective(s) of the study. The committee recommendations and actions taken by the investigator in response to the recommendations are submitted with the protocol to the HUC.

(4) When applicable, the protocol or test plan will be submitted to the radioisotope/radiation control committee, or equivalent, established in accordance with TB MED 525. The committee recommendations and actions taken by the investigator in response to those recommendations are submitted with the protocol to the HUC.

(5) When applicable, the protocol will be submitted to the SSC–NCR for research which calls for the use of an attitude or opinion survey, as defined by AR 600–46. If such studies are planned, the SSC–NCR must be contacted to determine whether the survey requires approval of that Center. This information should accompany the proposal when it is submitted for review.Surveys that cross command lines or are sent to other Services require approval. Inquiries should be directed to Commander, SSC–NCR, Attitude and Opinion Survey Division, ATTN: ATNC–MOA,200 Stovall Street, Alexandria, VA 22332–0400 (AUTOVON 221–9680).

d. Informed consent documentation. The subject's agreement to participate in the study will be documented using DA Form 5303–R, or functional equivalent, in accordance with appendix E. If additional pages are required, plain bond paper will be used and each page will be initialed by the volunteer and the witness. This form is not appropriate for research performed by contract. The volunteer agreement will be written in language that is easily understood by the subject. In research conducted outside the United States involving non-U.S. citizens, a locally produced form in the subject's native language may be used. An English translation of the form will be provided to the HUC.

e. Protocol and/or test plan review after submission to the local HUC.

(1) *HUC actions.*

(a) The HUC determines the level of risk associated with the protocol or test plan.

(b) The HUC may make the following recommendations to the approving authority: Approved, approved with modification, defer review to higher authority, disapproved, or exempt from further human use review.

(c) The HUC requires that the information given to subjects as a part of the informed consent is in accordance with the applicable portions of appendix E. The committee may require that information, in addition to that specifically mentioned in appendix E, be given to the subject when, in the HUC's judgement, the information would meaningfully add to the protection of the rights and welfare of the subject.

(d) The HUC reviews research involving minors. The committee will determine if assent is required and establish the method documenting such assent. The committee may waive the requirement for assent provided the HUC finds and documents that the research could not practicably be carried out without the waiver (see para 3–1*o*(4)).

(e) The HUC reviews research involving wards of a State agency, and other vulnerable categories of human subjects. The HUC determines if the use of such a category of subjects is warranted.If, in the opinion of the committee, the use of this category of subjects is appropriate, then the protocol is forwarded through command channels to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012, for approval.

(f) The HUC conducts a continuing review of the research approved by the HUC at intervals appropriate to the level of risk, but at least annually. The format for the review (for example, progress report from the investigator) will be determined by the HUC.

(g) A HUC reviews research involving medical devices.If, in the opinion of the HUC, the device does not pose a significant risk to the research subject, the organization will not be required to submit an IDE to the FDA.

(h) Certain categories of research may be reviewed by the HUC using the expedited review procedures in *g*below.

(i) Exempt categories of research are discussed in appendix F.

(2) *Approving official actions.* Approving officials—

(a) Will accept or reject the recommendations of the HUC. Safeguards or special restrictions imposed on a protocol by a HUC may not be reduced or waived by approving officials upon approval of the protocol or test plan.

(b) May require additional safeguards, may disapprove the protocol or test plan, or may refer it to a higher review committee and approving authority.

(c) Appoint a medical monitor (see glossary) for all studies that are greater than minimal risk.

(d) Obtain a health hazard assessment prior to approving a research protocol or test plan involving human subjects in the operation of military materiel.

(e) Notify the investigator of their decision to approve or disapprove the research proposal, or of modifications required to secure approval.

(f) Ensure the continued evaluation of research programs by the program or project manager or equivalent official to assure that the policies and procedures established by this regulation are being followed.

(g) Will, when higher approval authority is required, forward two

copies of the research protocol or test plan, informed consent documentation (DA Form 5303–R, or functional equivalent if applicable), all minutes of committees reviewing the protocol, and the commander's recommendations through command channels to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

f. Actions taken by an organization without a local HUC.

(1) The investigator accomplishes the actions noted in *c* above.

(2) The commander or organizational head accomplishes the actions noted in *e(2)(d)* above, and forwards the protocol with his or her recommendations, through the military chain of command, to the next level of command having an approved HUC.

g. Expedited review procedures. These procedures are as follows:

(1) Research activities involving no more than minimal risk and in which the only involvement of human subjects will be in one or more of the categories listed at appendix D may be reviewed by the HUC through the expedited review procedure.

(2) The HUC may also use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Under an expedited review procedure, the HUC chairman or one or more HUC reviewers designated by the chairman may carry out the review. The reviewers may exercise all of the authorities of the HUC except that of disapproval. Research may be disapproved only after review according to the nonexpedited procedure in *e* above.

(3) Each HUC using an expedited review procedure adopts a method for keeping all members and the commander advised of approved proposals.

(4) The approving official may restrict, suspend, or end a HUC's use of the expedited review procedure when necessary to protect the rights or welfare of subjects.

h. Duty to warn. Commanders have an obligation to ensure that research volunteers are adequately informed concerning the risks involved with their participation in research, and to provide them with any newly acquired information that may affect their well-being when that information becomes available.The duty to warn exists even after the individual volunteer has completed his or her participation in research. To accomplish this, the MACOM or agency conducting or sponsoring research must establish a system which will permit the identification of volunteers who have participated in research conducted or sponsored by that command or agency, and take actions to notify volunteers of newly acquired information. (See *a* above.)

i. Determining responsibility for review of protocols when more than one DOD or DA component is involved. The commander will determine primary responsibility based upon consideration of whether the subjects are inpatients or outpatients of a DOD medical treatment facility (MTF); whether the study is conducted in-house or by contract; or whether the prospective subjects are members of a DOD component.

(1) When the research, regardless of in-house or contract status, involves use of patients in a DOD MTF, the component to which the MTF belongs organizationally will have primary responsibility;except as provided in (3) below.

(2) For research not involving the use of inpatients at a DOD MTF, primary responsibility rests as follows:

(a) If the research is done on grant or contract, primary responsibility rests with the component providing funds.

(b) If research is conducted in-house, primary responsibility rests with the component to which the principal investigator is assigned.

(c) If research is not funded by a DOD or DA component and there is no DOD or DA principal investigator, primary responsibility rests with the component to which the prospective human subject is assigned.

(3) Studies funded by the Uniformed Services University of the Health Sciences (USUHS) or the Defense Nuclear Agency are reviewed and approved in accordance with policies established by the funding activity, and DODD 3216.2.

j. Records. Organizations or agencies conducting research involving volunteers will maintain records in accordance with AR 25–400–2, which are pertinent to the research conducted.These records will include, at a minimum—

(1) Documentation of approval to conduct the study.

(2) A copy of the approved protocol or test plan.

(3) The volunteer's signed informed consent (for example, DA Form 5303–R).

(4) A summary of the results of the research, to include any untoward reactions or occurrences. (See app H for a discussion of the composition of the Volunteer Data Base.)

k. Contractors or grantees. Contractors or grantees holding an approved Department of Health and Human Services(DHHS) Form HHS 596 (Protection of Human Subjects Assurance/Certification/ Declaration) are considered in compliance with this regulation. (See fig 3–1 for sample DHHS Form HHS 596.) In the absence of such an assurance, a special assurance will be negotiated by the contracting officer with the contractor or grantee. Organizations can verify that a contractor has a valid DHHS Form HHS 596 by contacting the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S.Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012. Even though a contractor has a review process which is consistent with Federal law (that is, 45 CFR 46), it is incumbent upon the approving official to administratively review the protocol to assure that it complies with the policies established in this regulation.

l. Technical reports and publications.

(1) Technical reports will be prepared in accordance with AR 70–31 and follow the format established in MIL–STD 847B or its revisions.

(2) Publications regarding the results of DA conducted research will be released by the approving official in accordance with the provisions of AR 360–5 and will contain the following statement: "The investigators have adhered to the policies for protection of human subjects as prescribed in AR 70–25."

(3) Publications regarding the results of DA sponsored research conducted by contract or grant will note adherence with 45 CFR 46, as amended.

m. Requests for exceptions to policy. Requests for exceptions to policy are submitted to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012. Requests will then be submitted to TSG's HSRRB for evaluation and recommendation to TSG; and TSG's recommendation to the ASD (HA) or USD (A), as appropriate.

SAMPLE

OMB No. 0925-0037

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☒ ORIGINAL ☐ FOLLOWUP ☐ EXEMPTION (previously undesignated)

☐ GRANT ☒ CONTRACT ☐ FELLOW ☐ OTHER

☐ New ☐ Competing continuation ☐ Noncompeting continuation ☐ Supplemental

APPLICATION IDENTIFICATION NO. *(If known)*

POLICY: A research activity involving human subjects that is not exempt from HHS regulations may not be funded unless an Institutional Review Board (IRB) has reviewed and approved the activity in accordance with Section 474 of the Public Health Service Act as implemented by Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46—as revised). The applicant institution must submit certification of IRB approval to HHS unless the applicant institution has designated a specific exemption under Section 46.101(b) which applies to the proposed research activity. Institutions with an assurance of compliance on file with HHS which covers the proposed activity should submit certification of IRB review and approval with each application. (In exceptional cases, certification may be accepted up to 60 days after the receipt date for which the application is submitted.) In the case of institutions which do not have an assurance of compliance on file with HHS covering the proposed activity, certification of IRB review and approval must be submitted within 30 days of the receipt of a written request from HHS for certification.

1. TITLE OF APPLICATION OR ACTIVITY

Evaluation of Mefloquine in the Treatment of P.falciparum malaria

2. PRINCIPAL INVESTIGATOR, PROGRAM DIRECTOR, OR FELLOW

John Boslego, MD

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION *(see reverse side)*

4. HHS ASSURANCE STATUS

☒ This institution has an approved assurance of compliance on file with HHS which covers this activity.

M1369 Assurance identification number _____ IRB identification number

☐ No assurance of compliance which applies to this activity has been established with HHS but the applicant institution will provide written assurance of compliance and certification of IRB review and approval in accordance with 45 CFR 46 upon request.

5. CERTIFICATION OF IRB REVIEW OR DECLARATION OF EXEMPTION

☒ This activity has been reviewed and approved by an IRB in accordance with the requirements of 45 CFR 46, including its relevant Subparts. This certification fulfills, when applicable, requirements for certifying FDA status for each investigational new drug or device *(see reverse side of this form)*.

Jul 31,1987 Date of IRB review and approval. *(If approval is pending, write "pending". Followup certification is required.)*
(month/day/year)

☒ Full Board Review ☐ Expedited Review

☐ This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by 45 CFR 46 will be reviewed and approved before they are initiated and that appropriate further certification *(Form HHS 596)* will be submitted.

☐ Human subjects are involved but this activity qualifies for exemption under 46.101(b) in accordance with paragraph _____ *(insert paragraph number of exemption in 46.101(b), 1 through 5)*, but the institution did not designate that exemption on the application.

6. Each official signing below certifies that the information provided on this form is correct and that each institution assumes responsibility for assuring required future reviews, approvals, and submissions of certification.

APPLICANT INSTITUTION	COOPERATING INSTITUTION
NAME, ADDRESS, AND TELEPHONE NO. Wonderful University PO Box 7 Anywhere, State 65473	NAME, ADDRESS, AND TELEPHONE NO.
NAME AND TITLE OF OFFICIAL *(print or type)* William D. Clyde, Jr Chancellor for Health Affairs	NAME AND TITLE OF OFFICIAL *(print or type)*
SIGNATURE OF OFFICIAL LISTED ABOVE *(and date)* William D. Clyde Jr 7Aug87	SIGNATURE OF OFFICIAL LISTED ABOVE *(and date)*

HHS 596 (Rev. 1/82) *(If additional space is needed, please use reverse side under "Items.")*

Figure 3-1. Sample DHHS Form HHS 596

SAMPLE

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION *(from front side)*

According to 45 CFR 46.121, if an application is made to HHS requiring certification and involving use of an investigational new drug or device, additional information is required. In addition, according to 21 CFR 312.1(a)(2), 30 days must elapse between date of receipt by FDA of Form FD-1571 and use of the drug, unless the 30 day delay period is waived by FDA.

3a. INVESTIGATIONAL NEW DRUG EXEMPTION *(if more than one is involved, list others below under NOTES):*

SPONSOR NAME

Hoffman LaRoche, Inc

DRUG NAME

Mefloquine, 250 mg tablet

DATE OF END OF 30-DAY EXPIRATION OR WAIVER	NUMBER ISSUED
1 Apr 85	IND 1423

3b. INVESTIGATIONAL DEVICE EXEMPTION:

SPONSOR NAME

DEVICE NAME

Unless notified otherwise by FDA, under 21 CFR 812.2(b) (ii) a sponsor is deemed to have an approved IDE if: (1) the IRB has agreed with the sponsor that the device is a nonsignificant risk device; and (2) the IRB has approved the study. *(Check applicable box.)*

☐ The IRB agrees with the sponsor that this device is a nonsignificant risk device.

OR

☐ The IDE application was submitted to FDA on *(date)* _____ . Number issued _____ .

NOTES:

HHS 596 (Rev. 1/93) BACK

GPO 843-135

Figure 3-1. Sample DHHS Form HHS 596—Continued

Appendix A
References

Section I
Required Publications

AR 25–400–2
The Modern Army Recordkeeping System (MARKS). (Cited in paras 3–2*j* and C–6*b*.)

AR 40–3
Medical, Dental, and Veterinary Care. (Cited in para 3–1*c*and *k*.)

AR 40–7
Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances. (Cited in paras 1–4*c*,2–9*c*(5), and 3–1*v*.)

AR 40–10
Health Hazard Assessment Program in Support of the Materiel Acquisition Decision Process. (Cited in para 2–8*d*.)

AR 70–10
Test and Evaluation During Development and Acquisition of Materiel.(Cited in para 2-8*d* and the glossary.)

AR 70–31
Standards for Technical Reporting. (Cited in para 3-2*l*(1).)

AR 71–3
User Testing. (Cited in para 3-1*t*.)

AR 335–15
Management Information Control System. (Cited in para 3-2*c*(1).)

AR 340–21
The Army Privacy Program. (Cited in paras 3-2*a*(4) and II-1.)

AR 360–5
Army Public Affairs, Public Information (Cited in paras 3-1*w* and 3-2*l*(2).)

AR 385–16
System Safety Engineering and Management.(Cited in para 2-8*d*.)

AR 600–46
Attitude and Opinion Survey Program. (Cited in paras 2-6, 2-9*c*(12), and 3-2*c*(5).)

AR 602–1
Human Factors Engineering Program. (Cited in para 2-8*d*.)

AR 602–2
Manpower and Personnel Integration (MANPRINT) in Materiel Acquisition Process. (Cited in para 2-8*d*.)

DA Pam 70–21
The Coordinated Test Program. (Cited in para 3-2*c*(1).)

DA Pam 71–3
Operational Testing and Evaluation Methodology and Procedures Guide.(Cited in para 3-2*c*(1).)

MIL–STD 847B
Format Requirements for Scientific and Technical Reports Prepared by or for the Department of Defense. (Cited in para 3-2*l*(1).) (This publication is available from the Naval Publications and Forms Center,5801 Tabor Avenue, Philadelphia, PA 19120-5099 using DD Form 1425(Specifications and Standards Requisition).)

TB MED 525
Occupational and Environmental Health Control of Hazards to Health from Ionizing Radiation Used by the Army Medical Department. (Cited in para 3-2*c*(4).)

Section II
Related Publications

A related publication is merely a source of additional information. The user does not have to read it to understand this regulation.

AR 11–2
Internal Control Systems

AR 40–38
Clinical Investigation Program

AR 40–66
Medical Record and Quality Assurance Administration

AR 70–14
Publication and Reprints of Articles in Professional Journals

AR 70–65
Management of Controlled Substances, Ethyl Alcohol, and Hazardous Biological Substances in Army Research, Development, Test, and Evaluation Facilities

AR 600–50
Standards of Conduct for Department of the Army Personnel

AR 611–3
Army Occupational Survey Program (AOSP)

DODD 3216.2
Protection of Human Subjects in DOD-Supported Research. (To obtain this publication, see MIL-STD 847B, see I, above.)

DODD 6465.2
Organ Disposition After Autopsy. (To obtain this publication, see MIL-STD 847B see I, above.)

FM 3–9/AFR 355–7
Military Chemistry and Chemical Compounds

DHHS Regulation, 45 CFR 46
Protection of Human Subjects. (This publication is available from Commander, USAMRDC, ATTN: SGRD-HR, Fort Detrick, Frederick, MD 21701-5012.)

FDA Regulation 21 CFR subchapters A, D, and H
Food and Drugs. (This publication is available for reference at the local installation staff judge advocate office.)

Memorandum of Understanding between the FDA and DOD
Investigational Use of Drugs by Department of Defense, May 21, 1987. (This publication is available from the Commander, USAMRDC, ATTN: SGRD-HR, Fort Detrick, Frederick, MD 21701-5012.)

10 USC 980
Limitation on the Use of Humans as Experimental Subjects.(This publication is available for reference at the local installation staff judge advocate office.)

10 USC 1102
Restriction on the Use of Information Obtained During Certain Epidemiologic-Assessment Interviews. (This publication is available for reference at the local installation staff judge advocate office.)

Unnumbered Publication
Convention on the Prohibition of the Development, Production, and Stockpile of Bacteriological (Biological) and Toxin Weapons and on their Destruction, Article I. (This article is printed as a part of the publication entitled "Arms Control and Disarmament Agreements: Text and Histories of Negotiations", and is available from the U.S. Arms Control and Disarmament Agency, Washington, D.C. 20451.)

Section III
Prescribed Forms

DA Form 5303–R
Volunteer Agreement Affidavit. (Prescribed in para 3-2*c*(1).)

Section IV
Referenced Forms

DD Form 1425
Specifications and Standards Requisition

DHHS Form HHS 596
Protection of Human Subjects Assurance/Certification/ Declaration.(Only the contractor or grantee will obtain and use this form. This form after approval, however, is shown to the contracting officer as proof of the contractor's or grantee's compliance with this regulation. See para 3-2*k*, fig 3-1, and the glossary.)

Appendix B
Guidelines for Preparation of Research Protocol and/or Test Plan

B–1. Project title
Enter complete project title. (If an amendment, the words "Amendment to. . . . . ." must precede the project title.)

B–2. Investigators
a. Principal investigator.
b. Associate investigators.

B–3. Location of study
List of facilities to be used.

B–4. Time required to complete
Give month and year of expected start and completion dates.

B–5. Introduction
a. Synopsis.
(1) One-page summary of proposed study similar to the abstract of a scientific paper.
(2) Major safety concerns for human subjects briefly highlighted.
b. Military relevancy. Explain briefly the medical importance and possible usefulness of the project.
c. Objectives. State briefly, but specifically, the objectives of the project. Include items below when applicable.
(1) Study design.
(2) Type of subject population observed.
d. Status. State what has been accomplished or published in the proposed area of study. Describe the way in which the project will relate to, or differ from, that which has been accomplished.
e. Bibliography. List all references used in preparing the protocol.

B–6. Plan
Outline expected accomplishments in enough detail to show a clear course of action. Include technological validity of procedures and chronological steps to be taken. The plan should include, as a minimum, the information shown below on the study subjects.
a. Number of subjects. Give the total number of subjects expected to complete the study.
b. Age range.
c. Sex.
d. Inclusion criteria. Specific and detailed reasons for inclusion should be presented.
e. Diagnostic criteria for entry.
f. Evaluations before entry. Entries should include x ray, physical examinations, medical history, hematology, chemistry, and urinalysis as deemed appropriate.
g. Exclusion criteria. Include a complete list detailing the subjects, diseases, and medications that are excluded from the study.
h. Source of subjects. Describe briefly where the subjects will be obtained.
i. Subject identification. Describe the code system used.
j. Analysis of risks and benefits to subjects; risks to those conducting research.
k. Precautions to be taken to minimize or eliminate risks to subjects and those conducting the research.
l. Corrective action necessary.
m. Special medical care or equipment needed for subjects admitted to the project.

B–7. Evaluations made during and following the project
An evaluation may also be represented by using a project schematic. It is very important to identify in the protocol the person who will perform the evaluations below.
a. Specimens to be collected.
(1) Amount and schedule of collections.
(2) Evaluations to be made on specimens.
(3) Storage. State where and if special conditions are required.
(4) Labeling and disposition.
(5) Laboratories performing evaluations.
(6) Special precautions for subject and investigators.
b. Clinical assessments. Include how adverse effects are to be recorded.
c. Vital signs. When desired and frequency.
d. Follow up procedures .
e. Disposition of data. State location and duration of storage.
f. Methods used for data collection. State critical measurements used as end points to characterize safety, efficacy, or equivalency.

B–8. Departure from protocol for individual patients
a. When allowed. Use flexible but definite criteria.
b. Who will be notified. (For example, patient, HUC, approving official.)

B–9. Incidents
a. Definition of incidents.
b. Immediate reporting.
c. Routine reporting.

B–10. Modification of protocol
Describe the procedure to be followed if the protocol is to be modified, terminated, or extended.

B–11. Examples of all forms to be used in the protocol

B–12. Use of information and publications arising from the study

B–13. Special or unusual funding implications

B–14. Name and telephone number of the medical monitor, when applicable

B–15. Human use committee
Brief explanation of which HUC will provide initial, continued, and annual review.

B–16. Signature of appropriate approving official and date

B–17. Documentation
a. Completed DA Form 5303–R.

b. Institutional review of scientific and human use issues.
c. HUC review with commander's approval.
d. Biographical sketch of principal and associate investigators.

Appendix C
Human Use Committees

C–1. Membership

a. Membership will include only full-time Federally employed persons.

b. Each HUC will have at least five members. Members will have diverse backgrounds to ensure thorough review of research studies involving human volunteers as research subjects. Members should be sufficiently qualified through experience and expertise. *The racial and cultural backgrounds of members and their sensitivity* to such issues as community attitudes should ensure respect for their advice and counsel in safeguarding the rights and welfare of human subjects.

c. Besides having the professional competency to review research studies, the HUC will be able to determine if the proposed research is acceptable.Acceptability will be in terms of Army Medical Department (AMEDD) commitments and regulations, applicable law, and standards of conduct and practice. A HUC may review research periodically that involves vulnerable categories of human subjects (for example, those individuals with acute or severe physical or mental illness; or those who are economically or educationally disadvantaged). Therefore, it will include one or more persons concerned primarily with the welfare of these subjects.

d. Normally, no HUC may consist entirely of men or women, or members of one profession. However, the approving official may waive this requirement in those cases in which compliance is impractical.

e. Each HUC will include at least one member whose primary concerns are nonscientific; for example, lawyers, ethicists, and members of the clergy.Should a given proposal include more than minimal risk, a physician will be included as an ad hoc member of the committee.

f. Each HUC will include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person affiliated with the institution. This requirement may be met by appointing a member of an institution or organizational unit not subject to the immediate authority of the approving official.

g. Except to provide information requested by the HUC, no HUC member may take part in a review of any project in which the member serves as the principal investigator or associate investigator.

h. A HUC may invite persons with special competence to assist in the review of complex issues that require expertise beyond that available on the HUC. These persons may not vote with the HUC.

i. The approving official may not be a member. The approving official may not approve research for which he or she is also a principal or associate investigator. A higher echelon of command must review and approve such research projects.

C–2. Functions and operations

Each HUC—

a. Will observe written procedures for the following:

(1) Conducting the initial and continuing review of the research.Included are reporting findings and actions to the investigator and the approving official.

(2) *Determining those projects that must be*—

(a) Reviewed more often than yearly.

(b) Verified from sources other than the investigators, that no material changes have occurred since the previous HUC review.

(3) Ensuring prompt reporting to the HUC of proposed changes in the research. Each HUC will ensure that changes in approved projects (during the period for which approval has already been given) are not initiated without HUC review except to eliminate immediate hazards to the subject.

(4) Ensuring prompt reporting to the HUC and approving official of unexpected problems involving risks to the subjects or others.

b. Will review proposed protocols at meetings attended by a majority of members except when an expedited review is used (see C–3 below). For the protocol to be approved, it will receive the approval of a majority of those members present.

c. Will report to the approving official any serious or continuing noncompliance with HUC requirements and determinations found by investigators.

d. Will conduct continuing review of research studies at intervals proper to the degree of risk, but not less than once per year.

e. Will have the authority to observe or have a third party observe the consent process and the investigation.

f. Will maintain a current list of HUC members. Members will be identified by name, earned degrees, representative capacity and, experience such as board certificates and licenses. The information will be complete enough to describe each member's chief expected contributions to HUC reviews.Any employment or other relationship between members and the institution will be noted.

g. May recommend safeguards or special conditions to a protocol.If the HUC does so, the approving official may take the following action:

(1) Not reduce the safeguards or conditions if he or she approves the protocol.

(2) Require additional safeguards.

(3) Disapprove the protocol.

(4) Refer the protocol to a higher echelon approving authority and review committee.

C–3. *Expedited review procedures*

a. See appendix D for a list of categories of investigations that the HUC may review in an expedited review procedure.

b. See paragraph 3–2*g* for the expedited review procedure that the HUC will follow.

C–4. Criteria for HUC approval of activities/investigations requiring volunteers

a. In evaluating risks and benefits for research investigations, the HUC should consider only those that may result from the investigation.

b. To approve investigations covered by this regulation, the HUC will determine that all of the requirements below are met.

(1) Risks to subjects are minimized by using procedures that are—

(a) Consistent with sound investigation design and do not unnecessarily expose subjects to risk.

(b) Already being used on the subjects for diagnosis or treatment, when appropriate.

(2) Risks to subjects are reasonable in relation to anticipated benefits to subjects.

(3) In making an assessment for the selection of subjects, the HUC should take into account the—

(a) Purpose of the investigation.

(b) Setting in which the research investigation will be conducted.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

(5) Informed consent will be properly documented.

(6) The plan makes adequate provision for monitoring the data collected to ensure the safety of subjects when appropriate.

(7) Adequate provisions exist to protect the privacy of subjects and to maintain the confidentiality of data when appropriate.

c. Some or all of the subjects may be vulnerable to coercion or undue influence such as persons with acute or severe physical or mental illness, or those who are economically or educationally disadvantaged. If so, proper additional safeguards will be included in the study to protect the rights and welfare of these subjects.

C–5. Suspension or termination of approved research investigation

a. A HUC will have the authority to suspend or end an approved investigation that—

(1) Is not being conducted according to the HUC's requirements.

(2) Has been associated with unexpected serious harm to subjects.

b. Suspensions or terminations of research will include a statement of the reasons for the HUC's action. They will be reported promptly to the principal investigator and approval official.

C–6. HUC records

a. A HUC will prepare and maintain adequate documents on HUC activities, including—

(1) Copies of all protocols reviewed, scientific evaluations that accompany the proposals, approved sample consent documents, progress reports submitted by investigators and reports of injuries and adverse reactions.

(2) Minutes of HUC meetings showing attendance; actions taken by the HUC; the vote on these actions, including the number of members voting for, against, and abstaining on a decision; the basis for requiring changes or disapproving the investigation; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the HUC and the investigators.

(5) A list of HUC members.

(6) Written procedures for the HUC.

(7) Statements of significant new findings.

b. The records required by this regulation will be retained permanently (see AR 25–400–2). Such records will be reasonably accessible for inspection and copying by authorized DA personnel and representatives of the FDA.

C–7. Conflict of interest

a. It is essential that the members of the HUC continue to be perceived and, in fact, are free from conflict of interest in their daily duties and especially in regards to the protocols they review.

b. The issue of conflict of interest has been addressed by public law, DOD directive, and Army regulation. The situations discussed below are merely examples of the types of activities and relationships which may result in conflict or the appearance of conflicts of interest. They are by no means the only ways that conflicts arise.

(1) *The potential for personal or financial gain.* A committee member who is deliberating a protocol which is to be performed by a contractor, in which the member or a member of his or her immediate family is a corporate officer, stockholder, consultant or employee, could be accused of conflict of interest if he or she voted on the protocol, regardless of his or her vote.

(2) *The potential for personal reward.* A committee member who is affiliated with a protocol in the capacity of principal, associate or co-investigator, could be accused of conflict of interest if he or she voted on the protocol, regardless of his or her vote.

(3) *Command influence.* The mission (for example, the purpose of the research) should not override or obscure its methods. It is imperative that the committee, through its members, continue to be recognized as a reasonable, deliberative body, whose bias is the safety and welfare of the research subject.It is incumbent upon each committee member to assure his or her concerns regarding the moral, ethical, and legal issues of each protocol are answered to his or her satisfaction before voting according to his or her conscience.

c. Commanders and organizational heads will establish a method to ensure that each committee member is familiar with the pertinent laws and regulatory guidance regarding conflict of interest.

C–8. Legal review

Prior to establishing a HUC, the commander or organizational head will obtain legal counsel from the staff judge advocate.

Appendix D
Expedited Review Categories

D–1. Hair, nails, teeth

Collection of—

a. Hair and nail clippings in a nondisfiguring way.

b. Deciduous teeth.

c. Permanent teeth if patient care indicates a need for extraction.

D–2. Excreta and secretions

Collection of—

a. Excreta and external secretions including sweat and uncannulated saliva.

b. Placenta at delivery.

c. Amniotic fluid at the time of rupture of the membrane before or during labor.

D–3. Physical data

Recording of data from subjects who are 18 years of age or older, using noninvasive procedures routinely employed in clinical practice. This category—

a. Includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy.

b. Includes such procedures as—

(1) Weighing.

(2) Electrocardiography.

(3) Electroencephalography.

(4) Thermography.

(5) Detection of naturally occurring radioactivity.

(6) Diagnostic echography.

(7) Electroretinography.

c. Does not include exposure to electromagnetic radiation outside the visible range (for example, x rays or microwaves).

D–4. Blood

Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an 8-week period and no more often than two times per week.Subjects will be 18 years of age or older, in good health, and not pregnant.

D–5. Dental plaque and calculus

Collection of both supragingival and subgingival dental plaque and calculus.The procedure must not be more invasive than routine prophylactic scaling of the teeth. The process must be accomplished according to accepted prophylactic techniques.

D–6. Voice records

Voice recordings made for research purposes such as investigations of speech defects.

D–7. Exercise

Moderate exercise by healthy volunteers.

D–8. Existing data

Study of existing data, documents, records, or pathological or diagnostic specimens.

D–9. Behavior

Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or

test development, where the investigator does not manipulate the subject's behavior and research will not involve stress to subjects.

Appendix E
Instructions for the Completion of the Volunteer Agreement Affidavit

E–1. Title and location
The title of the study and place where it is to be conducted.

E–2. Principal Investigator
The name of the principal investigator conducting the study.

E–3. Description of the study
A statement that the study involves research. An explanation of the purpose of the study and the expected duration of the subject's participation. A description of the procedures to be followed. An identification of any experimental procedures. A statement giving information about prior, similar, or related studies that provide the rationale for this study.

E–4. Risks
A description of any reasonably foreseeable risks or discomforts to the subject.

E–5. Benefits
A description of the benefits, if any, to the subject or to others that may reasonably be expected from the study. If there is no benefit to the subject, it should be so stated.

E–6. Alternative treatment
When applicable, a disclosure of proper alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

E–7. Confidentiality
A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. Also, in the case of an investigational drug or medical device protocol, a statement noting that the FDA may inspect the records. If the study is being performed by a contractor, a statement noting that representatives of the DOD may inspect the records.

E–8. Points of contact
An explanation of whom to contact for answers to pertinent questions about the study and the study subject's rights, and whom to contact in the event of a study-related injury to the subject. This should include a name or office and the commercial and AUTOVON telephone numbers.

E–9. Subject's rights
A statement that—

a. Participation is voluntary.

b. Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.

c. The subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

E–10. Compensation
For a study involving more than minimal risk, an explanation as to whether any compensation and medical treatment are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

E–11. Cautions
When appropriate, one or more of the elements of information below will also be given to each subject.

a. A statement that a certain treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant) that are currently unforeseeable. (Possible genetic effects to the offspring of males should be addressed when applicable.)

b. The anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

c. Any additional costs to the subject that may result from participation in the study.

d. The consequences of a subject's decision to withdraw from the study and procedures for the orderly end of the subject's participation.

e. A statement that new findings developed during the course of the study which could affect the subject's willingness to continue will be given to the subject.

f. The approximate number of subjects involved in the study.

g. The precautions to be observed by the subject before and after the study.

h. If photographs are to be taken, the degree to which actions will be taken to protect the identity of the subject.

i. A statement as to whether the results of the research will be made known to the subject.

E–12. Disposition of the informed consent
The principal investigator will retain the original signed informed consent.A copy will be provided to the volunteer. If the volunteer consents, the investigator will provide a copy of the signed DA Form 5303–R to the medical records custodian for inclusion in the volunteer's medical treatment record(AR 40–66, para 6–2*f*.)

Appendix F
Exemptions

F–1. Exempt activities
Activities in which human subjects are involved in one or more of the categories below are exempt from this regulation.

a. Routine epidemiological surveys that are of no more than minimal risk as set forth in the human protection regulations issued by the DHHS (45 CFR 46). (See the glossary for the definition of epidemiological survey.)

b. Research in educational settings which involves normal educational practices such as—

(1) Regular and special education strategies.

(2) The effectiveness of, or the comparison among, techniques of instruction, curricula, or classroom management methods.

c. Research that involves the use of educational tests when the data is recorded in such a way that subjects cannot be identified directly or indirectly.

d. Research that involves survey, interview procedures, or the observation of public behavior (including observation by participants) except where all the following exist:

(1) Responses or observations are recorded in such a way that subjects can be identified directly or indirectly.

(2) The subject's responses or recorded observations, if they become known outside the research, could reasonably place the subject at risk of criminal or civil liability, or would damage the subject's financial standing or employability.

(3) The research deals with sensitive aspects of the subject's behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol.

e. Research involving the collection or study of existing data, documents, records, or pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded in such a way that subjects cannot be identified directly or indirectly.

f. Individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercise (for example, Army Training and Evaluation Program (*ARTEP*), *Skill* Qualification Test (SQT)). Evaluation of the training's effect on the individual participants may or may not be exempt depending on

how the evaluation is made (for example, drawing of blood is not exempt).

g. Job related tasks of military or civilian personnel who are qualified to test by duty assignments that call specifically for such qualifications.

h. Inclusion of human subjects as the indirect object of research involving minimal risk or less in the development and testing of military weapon systems, vehicles, aircraft, and other material are exempt from the requirement for obtaining informed consent from the participants. The determination of whether a proposal is minimal risk or less is made by a HUC established in accordance with paragraph 3–2*b* of this regulation.

i. Other research which is exempted by future changes to DHHS regulations, and which is consistent with this regulation and DOD Directive 3216.2.

F–2. Not used

Appendix G
Legal Implications

G–1. Authority
The Secretary of the Army is authorized to conduct research and development programs including the procurement of services that are needed for these programs (10 USC 4503). The Secretary has the authority to "assign, detail and prescribe the duties"of the members of the Army and civilian personnel (10 USC 3013).

G–2. Military personnel and Department of the Army civilian employees
Compensation for the disability or death of a civilian employee resulting from personal injury or disease proximately caused by employment is payable under the Federal Employees Compensation Act (5 USC 8100 et seq.), regardless of whether employment was of a hazardous nature. The amount and type of disability compensation or other benefits payable by reason of the death or disability of a member of the Army resulting from injury or disease incident to service depends upon the individual status of each member, and is covered by various provisions of law. It may be stated generally that under present laws no additional rights against the government will result from the death or disability of military and civilian personnel participating in experiments by reason of the hazardous nature of the operations.

G–3. Private citizens
It is the policy of the United States to prohibit the acceptance of voluntary services (31 USC 1342). Individuals may, however, enter into an independent contractual relationship and participate for compensation as authorized by applicable directives (for example, volume 45 Decision of the Comptroller General, 1966, p. 649 (45 DCG 649)). Accordingly, any such service should be accompanied by a statement to the effect that the individual will not receive or become entitled to any compensation other than that stated in the contract for these services.

G–4. Use of appropriated funds for the purchase of insurance
Since the payment of insurance premiums on the life of an officer or employee of the United States is a form of compensation which is not currently authorized, payment of those premiums is prohibited.

G–5. Contractor's employees
There appears to be no legal objection to the use of employees of contractors in research and development experiments. It is the responsibility of the contracting officer to determine whether the terms of the contract are sufficiently broad to permit the participation of these employees. Generally, benefits to which contract employees may become entitled by reason of death or disability resulting from their employment are payable under State Workmen's Compensation law, except persons covered by the survivor's insurance provisions of the Social Security Act (42 USC 402). Reimbursement of the employer for additional costs by reason of this liability for his or her employees will depend upon the terms of each contract. These employees are not disqualified from prosecuting claims against the government under the Federal Torts Claim Act (28 USC 2671 et seq.), if such a claim exists.

G–6. Irregular or fee-basis employees
Intermittent services of such employees are authorized. (Experts and consultants, 5 USC 3109(b) and Sec. 710 Defense Production Act of 1960 (64 Stat. 819, 50 USC App 2160); and for architects, engineers, and other technical and professional personnel on a fee-basis, 10 USC 4540.) Whether these employees can be detailed or assigned to the proposed experiments will depend upon the statutory authority for employment and the provisions of their employment agreement in each case. The Federal Employees Compensation Act, *supra*, in all probability applies with respect to these irregular and fee-basis employees for any injury or disease resulting from their employment, although a final determination in such cases will have to be made by the Federal agency responsible for deciding claims. Subject to such restrictions and limitations as may appear in the statutory authority under which he or she is employed, it would appear that the Government may legally bear the expense of premiums upon the life of an irregular or fee-basis employee whose rate of compensation is not fixed by law or regulations. In this regard, it may be advisable for the government to provide an additional allowance to the employee for financing such private insurance arrangements as he or she may wish to make rather than to undertake direct negotiations with insurance carriers for the desired coverage.

Appendix H
Volunteer Data Base

H–1. General
The intent of the data base is twofold: first, to readily answer questions concerning an individual's participation in research conducted or sponsored by the command; and second, to ensure that the command can exercise its "duty to warn." The data base must contain items of personal information, for example, name, social security number (SSN), etc., which subjects it to the provisions of The Privacy Act of 1974. AR 340–21 addresses the requirements for establishing such a system of records. For assistance in developing the systems notice for publication in the Federal Register, contact Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012, AUTOVON 343–2165.

H–2. Data elements
The elements listed below are representative of those items that could be found in such a data base. It is not meant to be all inclusive, and can be modified to meet individual command needs.

a. Records of the study. A copy of the—

(1) Approved test plan or protocol.

(2) Letter or other document approving the conduct of the test or protocol.

(3) Signed informed consent for each volunteer.

(4) Report generated by the results of the test or protocol.

b. Data elements—volunteer's personal information.

(1) Name.

(2) Rank (if applicable).

(3) SSN.

(4) Sex.

(5) Date of birth.

(6) MOS or AOC (if applicable).

(7) Local address and telephone number.

(8) Permanent address and telephone number.

(9) Unit (if applicable).

c. Data elements—test plan or protocol information.

(1) Test or protocol title.
(2) Principal investigator's name.
(3) Laboratory, unit, or facility conducting the test protocol.
(4) Location of the test.
(5) Test period.
(6) Challenge material data (if applicable).
(a) Name of the material used (both active and inert material).
(b) Manufacturer.
(c) Lot number.
(d) Expiration date.
(e) IND or IDE number.
(7) Date the volunteer completed or withdrew from the study.
(8) Reason for withdrawal (if applicable).
(9) Description of untoward reactions experienced by the volunteer (if none, so state).

H–3. Updating perishable data

Selected items of personal information are perishable; for example, local address and telephone number. A method should be established, which is consistent with the potential for long-term risks of the test or protocol, to update this information. For example, the risks associated with testing a new parachute will be readily apparent; whereas the risks associated with the testing of new, obscurant smoke may not be known for some time to come.

Glossary

Section I
Abbreviations

AIDS
Acquired immune deficiency syndrome

AMEDD
Army Medical Department

AOC
area of concentration

ARNG
Army National Guard

ARTEP
Army Training and Evaluation Program

ASA (RDA)
Assistant Secretary of the Army (Research, Development, and Acquisition)

ASD (HA)
Assistant Secretary of Defense (Health Affairs)

CFR
Code of Federal Regulations

DA
Department of the Army

DCSPER
Deputy Chief of Staff for Personnel

DHHS
Department of Health and Human Services

DOD
Department of Defense

DTF
dental treatment facility

FDA
Food and Drug Administration

HIV
human immunodeficiency virus

HSRRB
Human Subjects Research Review Board

HUC
human use committee

HURRAO
Human Use Review and Regulatory Affairs Office

IDE
Investigational Device Exemption

IND
Notice of Claimed Investigational Exemption for a New Drug

IRB
institutional review board

MACOM
major Army command

MOS
military occupation specialty

MTF
medical treatment facility

NDA
New Drug Application

OTSG
Office of the Surgeon General

PCS
permanent change of station

PI
principal investigator

RDTE
research, development, test, and evaluation

SI
skill identifier

SSC–NCR
Soldier Support Center—National Capital Region

SSN
social security number

SQT
skill qualification test

TSG
The Surgeon General

USAMRDC
U.S. Army Medical Research and Development Command

USAR
U.S. Army Reserve

USD (A)
Under Secretary of Defense for Acquisition

USUHS
Uniformed Services University of the Health Sciences

Section II
Terms

Adverse personnel action
For the purposes of paragraph 3–11, this term includes—

a. A court martial.
b. Non-judicial punishment.
c. Involuntary separation (other than for medical reasons).
d. Administrative or punitive reduction in grade.
e. Denial of promotion.
f. An unfavorable entry in a personnel record.
g. A bar to reenlistment.
h. Any other action considered by the DA to be an adverse personnel action.

Approving official
A military commander or civilian director of an organizational element of a DA component who has been delegated authority to approve the use of human subjects in research.

Assent
A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Associate investigator
A person who may be involved in the execution of research, but does not have overall primary responsibility. The FDA refers to such an individual as a subinvestigator.

Certificate of Assurance
See Protection of Human Subjects Assurance/Certification/Declaration.

Chemical warfare agent (FM 3–9)
A chemical compound which, through its chemical properties, produces lethal or damaging effects on man. Excluded from consideration are riot control agents, anti-plant agents, and smoke and flame materials.

a. Chemical agents may be grouped according to use:

(1) *Toxic chemical agents.* Agents capable of producing incapacitation, serious injury, or death when used in field concentrations.

(2) *Incapacitating agents.* Agents that produce physiological or mental effects or both that may persist for hours or days after exposure, rendering individuals incapable of concerted efforts in the performance of their assigned duties. Complete recovery of incapacitating agent casualties is expected without medical treatment.

b. Nonchemical warfare agents may be grouped according to use as follows:

(1) Riot control agents. Compounds widely used by governments for domestic law purposes, and which produce transient effects on man that disappear minutes after removal from exposure.
(2) Training agents and compounds.
(3) Screening and signaling smokes.
(4) Anti-plant agents.

c. It should be noted that the Convention on the Prohibition of the Development, Production, and Stockpile of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, Article I, dated 26 March 1975, stipulates that—

"Each State Party to this Convention undertakes never in any circumstance to develop, produce, stockpile, or otherwise acquire or retain:

(1) Microbial and other biological agents or toxins whatever their origin or method of production, of types or in quantities that have no justification for prophylactic, protective or other peaceful purposes;

(2) Weapons, equipment, or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict." Accordingly, chemical materials obtained from such sources or processes are considered biological, not chemical, weapons.

Clinical investigation
An organized inquiry into health problems for all conditions that are of concern in providing health care to beneficiaries of the military health care system, including active duty personnel, dependents, and retired personnel. The clinical investigation program is described in AR 40–38.

Consent
See informed consent.

Development
Systematic use of scientific knowledge, directed toward—

a. Significant improvements in or creation of useful products to meet specific performance requirements.

b. Development of components for incorporation in end items to meet specific performance requirements.

c. Construction of hardware for test purposes to determine feasibility of technical approaches.

d. Formulation and refinement of techniques and procedures which improve Army capabilities in nonmateriel areas.

Epidemiologic-assessment interview
For the purpose of paragraph 3–1*l*, this term means questioning of a serum positive member of the Armed Forces for the purposes of medical treatment or counseling, or for epidemiologic or statistical purposes.

Epidemiological surveys
For the purpose of this regulation, the term means studies of the distribution and determinants of disease frequency in humans, involving no more that minimal risk in which research data is not linked to personal identifiers.Epidemiological surveys focus on "ills" of a population rather than on persons.

Evaluation
The subjective determination of the military value of a hardware item or system, real or conceptual, to the user. There are three types of evaluation:Developer, technical, and operational. See 70–10 for more detail.

Expedited review procedures
Those procedures used in research involving no more than minimal risk and those used for minor changes in approved investigations (see app D).These procedures minimize time required for review.

Experimental subject
See Human subject.

Health care personnel
Military personnel, civilian employees, or contract personnel (including military and civilian staff members, assigned to, employed by, or appointed to the USUHS) who provide patient care or patient care support services in military MTFs and dental treatment facilities (DTFs).

Health care delivery study
Application of scientific methods to the study of availability, organization, administration, and management of health services. The efficiency and effectiveness with which such services are delivered are included.

Health and Human Services Certificate of Assurance
See Protection of Human Subjects Assurance/Certification/Declaration.

Human subject
a. A living individual about whom an investigator conducting research obtains data through interaction with the individual, including both physical procedures and manipulations of the subject or the subject's environment.The term does not include military or civilian personnel who are qualified to test by assignment to duties that call specifically for qualifications such as test pilots or test engineers.

b. Minor (child). A person who has not attained the legal age for consent to treatments or procedures involved in research, under the applicable laws and jurisdiction in which the research will be conducted.

c. Human subjects may be thought of as direct objects when the research is to determine the effects of a new system on humans (for example. the effects of a weapon's blast on hearing) as indirect objects when a test is conducted to determine how humans affect the ultimate performance of a system (doctrine concepts, training programs).

Human Subjects Research Review Board
The principal body of the Office of The Surgeon General (OTSG) for review of clinical investigation and research activities.

Human use committee
A body set up to provide initial and continuing review of research involving the use of human subjects. A HUC is fundamentally similar to an institutional review board (IRB) (45 CFR 46), but has somewhat different authority as compared to an IRB. Within DOD, authority to approve use of human subjects in research is vested in commanders. Commanders act on the recommendations of validly constituted HUCs. Outside DOD, IRBs tend to be vested with this authority. Appendix C describes the membership, functions, and operations of a HUC.

Informed consent
The legally effective agreement of the subject or subject's legally authorized representative for the subject to participate in research covered by this regulation. Informed consent includes, when appropriate, those elements listed in appendix E of this regulation.

a. Permission. The agreement of parent(s) or guardian to the participation of their child or ward in research.

b. Guardian. An individual who is authorized under applicable State or local law to consent on behalf of a minor (child) to general medical care.

c. Assent. A minor's(child's) affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Institution
Any public or private entity or agency (including Federal, State, or other agencies).

Investigational drug
A drug may be considered investigational when the composition is such that—

a. Its proposed use is not recognized for the use under the conditions prescribed; or its proposed use is not recommended or suggested in its approved labeling. Experts qualified by scientific training and experience evaluate the safety and effectiveness of drugs to make this determination.

b. Its use has become recognized as investigational, as a result of studies to determine its safety and effectiveness for use under such conditions.

Investigational medical device
a. A device that is not generally used in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans, and recognized as safe and effective.

b. Research is usually, but not necessarily, initiated to determine if the device is safe or effective.

Legally authorized representative
A person or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's taking apart in the procedures involved in the research.

Medical monitor
This person is a military or DA civilian physician qualified by the training and/or experience required to provide care to research subjects for conditions that may arise during the conduct of the research, and who monitors human subjects during the conduct of research. For the purpose of this regulation, the principal investigator may function as the medical monitor only in situations in which no other physician is available and approval for the principal investigator to function as medical monitor is granted by TSG. Requests for the principal investigator to function as the medical monitor will be sent to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012. In contractor performed research, a military or DA civilian

physician may be the medical monitor; however, this is usually a contractor provided resource.

Minimal risk
The proposed risks are not considered greater than these encountered in the subject's daily life or during routine physical or psychological examinations.

Non-U.S. citizens
Foreign nationals, excluding personnel on active duty.

Personal identifier
A method or system which links data to the individual from whom or about whom it pertains.

Principal investigator
A person, regardless of title, who is primarily responsible for the actual execution of the research.

Prisoner
Any person, (adult or minor) involuntarily confined or detained in a penal or correctional institution (for example, jail, workhouse, house of detention, prison, military stockade, or brig). The term is intended to encompass individuals detained pending arraignment, trial, or sentencing;and prisoners of war including detained personnel). The term does not include individuals voluntarily confined nor those persons subject to civil commitment procedures that are not alternatives to criminal prosecution.

Protection of Human Subjects Assurance/ Certification/Declaration
A document issued by the Office for Protection from Research risk, DHHS, in which that office acknowledges that a research institution has established policies and procedures consistent with 45 CFR 46.

Protocol
The written, detailed plan by which research is to be conducted. (See app B for an example of research protocol.) The plan contains, as a minimum— *a.* The objectives of the project.

b. The information to be collected.

c. The means by which it will be collected and evaluated; an assessment of potential risk and benefits to subjects; safety measures, and other means to be used to reduce any risk to subjects.

Radioisotope/radiation control committee
A committee appointed by the commander to ensure that individual users of radioactive materiels within the medical facility and each radionuclide will be approved and controlled. The approval and control is in accordance with the requirements specified in the conditions of the Nuclear Regulatory Commission license and DA radioactive material authorization and appropriate Federal directives.

Research
A systematic investigation that is designed to develop or contribute to generalizable knowledge. The term does not include individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises (DODD 3216.2)

Research, development, test, and evaluation
Includes those categories of research and development included in Program 6, Research and Development, and operational systems development contained in the Five-Year Defense Program.

Schedule I controlled drug substances
Any drug or substance by whatever official name, common or usual name, chemical name or brand name listed in 21 CFR 1308, for example, heroin.

Serum positive member of the Armed Forces
For the purposes of paragraph 3–1*l*, this term means a member of the Armed Forces who has been identified as having been exposed to a virus associated with the acquired immune deficiency syndrome (AIDS).

Subinvestigator
See associate investigator.

Test
A process by which data are accumulated to serve as a basis for assessing the degree to which an item or system meets, exceeds or fails to meet the technical or operational properties required. AR 70–10 has a more detailed discussion of the RDTE type test. There are no special terms.

RESERVED

VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 70-25 or AR 40-38; the proponent agency is OTSG

PRIVACY ACT OF 1974

Authority: 10 USC 3013, 44 USC 3101, and 10 USC 1071-1087.

Principle Purpose: To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.

Routine Uses: The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study; implementation of medical programs; adjudication of claims; and for the mandatory reporting of medical conditions as required by law. Information may be furnished to Federal, State and local agencies.

Disclosure: The furnishing of your SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A(1) - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, _____, SSN _____,

having full capacity to consent and having attained my _____birthday, do hereby volunteer/give consent as legal

representative for _____, to participate in _____

_____

(Research study)

_____

under the direction of _____

conducted at _____.

(Name of Institution)

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

_____.

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the rights of the person I represent on study-related injury, I may contact

_____

at _____

(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, I/the person I represent may be required (military volunteer) or requested *(civilian volunteer)* to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well-being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

_____

PART A (2) - ASSENT VOLUNTEER AFFIDAVIT *(MINOR CHILD)*

I, _____, SSN _____ having full

capacity to consent and having attained my _____ birthday, do hereby volunteer for _____

_____ to participate in _____

_____

(Research Study)

_____

under the direction of _____

conducted at _____.

(Name of Institution)

(Continue on Reverse)

PART A(2) - ASSENT VOLUNTEER AFFIDAVIT (*MINOR CHILD*) *(Cont'd.)*

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

_____

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights I may contact

_____

at _____

(Name, Address, and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my assent and withdraw from the study without further penalty or loss of benefits; however, I may be requested to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

_____

PART B - TO BE COMPLETED BY INVESTIGATOR

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: *(Provide a detailed explanation in accordance with Appendix C, AR 40-38 or AR 70-25.)*

I do ☐ **do not** ☐ *(check one & initial)* consent to the inclusion of this form in my outpatient medical treatment record.

SIGNATURE OF VOLUNTEER	DATE	SIGNATURE OF LEGAL GUARDIAN *(If volunteer is a minor)*
PERMANENT ADDRESS OF VOLUNTEER	TYPED NAME OF WITNESS	
	SIGNATURE OF WITNESS	DATE

REVERSE OF DA FORM 5303-R, MAY 88

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