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# **'Off the Rocker' and 'On the Floor': The Continued Development of Biochemical Incapacitating Weapons**

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MAKING KNOWLEDGE WORK

## **'Off the Rocker' and 'On the Floor': The Continued Development of Biochemical Incapacitating Weapons**

## **1.1 Introduction**

This paper explores the development of biochemical incapacitating agents and their delivery systems, which has been ongoing for over 55 years. It focuses on events in the United States, tracking the weapons programmes administered by the Department of Defense and related research efforts sponsored by the Department of Justice. Recent developments in several other countries are also discussed.

## **1.2 Definitions**

The longstanding military definition of an incapacitating agent is:

 $\dots$ a chemical agent which produces a temporary disabling condition that persists for hours to days after exposure to the agent (unlike that produced by riot control agents).<sup>1</sup>

From a military perspective, specific characteristics of such agents have been seen as follows:

(1) Highly potent (an extremely low dose is effective) and logistically feasible.

(2) Able to produce their effects by altering the higher regulatory activity of the central nervous system.

(3) Of a duration of action lasting hours or days, rather than of a momentary or fleeting action.

(4) Not seriously dangerous to life except at doses many times the effective dose.

(5) Not likely to produce permanent injury in concentrations which are militarily effective.<sup>2</sup>

However, contemporary definitions emphasise rapid onset of action and short duration of effects, characteristics which reflect the current preoccupation with counterterrorism and the associated convergence of military and policing requirements.<sup>3</sup> Generally for reasons of politics and public relations rather than accuracy these weapons have also been referred to as "calmatives" and "advanced riot control agents".<sup>4</sup> Particularly in the light of this intentionally cloudy terminology it is important to note that incapacitating agents are distinct from irritant chemical agents, often called riot control agents (RCAs), both in terms of their mechanism of action and their effects. Riot control agents act peripherally on the eyes, mucous membranes and skin, to produce local sensory irritant effects, whereas incapacitating agents act on receptors in the nervous system to produce central effects on cognition, perception and consciousness.

Whilst incapacitating agents have commonly been viewed as chemical weapons, the term 'biochemical weapon' is also used to reflect the confluence of chemistry and biology in this area.<sup>5</sup> As Dando and others have argued, greater understanding of biochemical processes in the body at the molecular level mean that it is now more appropriate to think of a biochemical threat spectrum rather than distinct chemical and biological weapons.<sup>6</sup> This is something that has been apparent for some considerable time. For example, in the late 1980's Douglass Jr. argued:

Prior distinctions between biological and chemical weapons have blurred. The two have merged, and the resulting "biochemical" weapons promise to emerge as the most sophisticated and potent weapons the world has ever seen.<sup>7</sup>

In this context Pearson's biochemical weapons spectrum is a useful concept, as shown in Table 1.

Classical CW	Industrial Pharmaceutical Chemicals	Bioregulators Peptides	Toxins	Genetically Modified BW	Traditional BW
Cyanide Phosgene Mustard Nerve Agents	Aerosols	Substance P Neurokinin A	Saxitoxin Ricin Botulinum Toxin Biological and Toxin	Modified/ Tailored Bacteria Viruses Weapons Conventior	Bacteria Viruses Rickettsia Anthrax Plague Tularemia
					<b>—</b>
	Chemical Weapo	ns Convention			
	Poison			Inf	ect
				1	

Table 1: The Biochemical Weapons Spectrum.<sup>8</sup>

Mid-spectrum agents are those that fall in between 'classical' chemical agents (i.e. nerve, blood, and blister agents) and biological agents (i.e. bacteria, viruses, and rickettsia) on this spectrum and share the characteristics of both chemical and biological weapons.<sup>9</sup> Such agents generally exert their effects through acting on particular cell receptors in the body and can have either a synthetic chemical origin (i.e. pharmaceuticals) or a natural biological origin (i.e. bioregulators, peptides, toxins). These mid-spectrum biochemical agents can have a variety of effects ranging from incapacitation to death, often determined by the dose, and can act on a variety of physiological processes, as described in a 2001 review paper:

Bioregulators are structurally diverse compounds that are capable of regulating a wide range of physiologic activities, such as bronchial and vascular tone, muscle contraction, blood pressure, heart rate, temperature, and immune responses.<sup>10</sup>

Sight should not be lost of the variety of biochemical pathways and systems that are potential targets for incapacitating agent development.<sup>11</sup> Nevertheless, the focus of "non-lethal" weapons development has long been biochemical agents that depress or inhibit the function of the central nervous system and this continues to be central to current investigations.<sup>12</sup> Neurotransmitters mediate chemical transmission in the nervous system through their interactions with specific receptors. In the central nervous system (CNS) these neurotransmitter-receptor interactions have a major role in regulating consciousness, mood, anxiety, perception, and cognition. Whilst neurotransmitters are the naturally occurring (bioregulatory) ligands that bind to cell receptors in the central nervous system, these receptors can also be bound by synthetic

chemicals (drugs/poisons). Amongst the latter there are a number of classes of agent under consideration as biochemical incapacitating weapons.<sup>13</sup>

## **1.3 Past Programmes**

## **1.3.1** Cold War Programme

Military interest in centrally acting biochemical agents as weapons, like other types of chemical and biological weapons, has a long history. The concept of employing chemical agents to cause temporary incapacitation rather than death is also an old one that began to receive greater attention as acceptance of lethal chemical agents declined in the aftermath of World War I.<sup>14</sup> However, it was not until after World War II that the expansion of the pharmaceutical industry led to the discovery of chemicals that would be suitable for this purpose<sup>15</sup> and interest from the US Army and the Central Intelligence Agency (CIA) soon followed.<sup>16</sup> SIPRI's 1971 study of Chemical and Biological Warfare noted:

The US Army's interest in psychochemicals was probably stimulated by the rapid development of psychotropic drugs by a number of chemical manufacturers after World War II. With the increasing use and availability of tranquilizers, stimulants and even hard drugs for the general public, it was perhaps inevitable that the possible military uses of the new substances should be investigated.<sup>17</sup>

A 1949 report by the US Army Chemical Corps ambitiously considered psychochemicals as alternatives to weapons of mass destruction (WMD), proposing three groups of potential incapacitating agents: LSD and related chemicals; tetrahydrocannabinol (THC) and analogues; and phenylethylamines.<sup>18</sup> The profound effects on the brain of LSD had only recently been discovered by accident during a pharmaceutical company's drug development process.<sup>19</sup> US Army-sponsored research began in 1951, which included the solicitation of candidate chemicals from various companies through its' Industrial Liaison Program.<sup>20</sup> Efforts focused on mescaline, LSD, and THC related chemicals and 45 different compounds had been studied by the end of 1955, 22 of which had been tested on animals.<sup>21</sup> During these early investigations a variety of mechanisms for incapacitation were considered in addition to psychotropic effects. These included agents that influenced blood pressure and thermoregulation, or induced anaesthesia, sedation, muscle paralysis, tremors, or emesis.<sup>22</sup> Broadly speaking agents were colloquially divided into "off the rocker" agents having psychotropic effects and "on the floor" agents causing incapacitation through effects on other physiological processes.<sup>23</sup> "Off the rocker" agents prevailed since the safety margins for other agents, including anaesthetic agents, sedatives, and opiate analgesics, were not considered sufficiently wide for them to perform as 'safe' military incapacitating agents.<sup>24</sup> Writing in 1971, Perry-Robinson noted:

The psychomimetics in fact seem to be one of the very few classes of incapacitating drug which have sufficient selectivity to give a wide enough margin of safety. Some of them are sufficiently potent for CW purposes.<sup>25</sup>

A 1955 report recommended continued development of psychochemical agents and human testing began in 1956 with research continuing to focus on the same three groups of agents. Tests on mescaline and derivatives found that too large a dose was required to induce incapacitating effects<sup>26</sup> and a candidate THC analogue was

discounted due to limited effects.<sup>27</sup> LSD remained the primary agent under investigation.<sup>28</sup> It was sufficiently potent but it too was later discounted due to its high production costs and side effects.<sup>29</sup> A large part of the US incapacitating agent programme consisted of scanning new chemicals emerging from industry with around 10,000 compounds screened by the US Army's Edgewood Arsenal each year.<sup>30</sup> In 1959 the Army began to investigate one such compound from the pharmaceutical industry called Sernyl, which was the chemical phencyclidine (PCP). Human tests were conducted and it was quickly approved for manufacturing as Agent SN despite its variable effects and the large doses required for incapacitation. However munitions containing SN were never produced.<sup>31</sup>

Another chemical that came to the attention of the programme around this time was 3quinuclidinyl benzilate, an anticholinergic glycollate agent that had been developed by Hoffman-La Roche Inc. in 1951. It acts by interfering with the transmission of acetylcholine, a major neurotransmitter, in the central nervous system. Designated Agent BZ, investigation and human testing began at Edgewood Arsenal and it soon became the primary agent under consideration,  $3^2$  capable of causing physical weakness, delirium and hallucinations in very small doses.<sup>33</sup> A re-evaluation of the US chemical and biological weapons programmes in 1961 led to priority being given to the development of an incapacitating chemical weapon capability and a project began to produce BZ munitions resulting in the standardization in March 1962 of the 750-lb M43 cluster bomb and the 175-lb M44 generator cluster, which released the solid BZ as a particulate smoke.<sup>34</sup> However, relatively few (around 1,500) of these munitions were stockpiled<sup>35</sup> and they were only ever considered interim weapons, never fully integrated into the US operational chemical weapons arsenal.<sup>36</sup> This was due to a number of shortcomings with both the agent and the delivery system ass Kirby has described:

...the operational problems that BZ presented were numerous. Its visible white agent cloud warned of its presence. Improvised masks, such as several layers of folded cloth over the nose and mouth could defeat it. Its envelope-of-action was less than ideal. The rate-of-action was delayed ..., and the duration of action was variable from 36 to 96 hours. Additionally, 50% to 80% of the casualties required restraint to prevent self-injury, and paranoia and mania were common personality traits during recovery. These uncertainties made BZ unattractive to military planners.<sup>37</sup>

Research into new incapacitating agents continued after the standardization of BZ and was broad in scope. For example, Pfizer was carrying out contracted research for the incapacitating agent programme considering various compounds including those that might induce retrograde amnesia.<sup>38</sup> By the late 1960's a number of different classes of compounds were under active investigation including: anaesthetics, analgesics, tranquilizing agents, anticholinergics (e.g. glycollates), and vomiting agents and the US Army's Edgewood Arsenal was also promoting the adoption of these agents for use in law enforcement.<sup>39</sup> Many of these agents under consideration at the time had been discounted earlier due to low safety margins.

Morphine-like opioid analgesics of interest to developers included a piperidinol compound given the code EA 3382 and a benzomorphan known as M-140. Research was ongoing to mix these compounds with antagonists<sup>I</sup> in order to improve their

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<sup>&</sup>lt;sup>I</sup> In pharmacology an agonist is defined as a drug that binds to a cell receptor to elicit certain effects. An antagonist is a drug that blocks the action of an agonist by binding to the same cell receptor.

safety margins. Tranquillizing agents under consideration included a phenothiazine compound called prolixin and a butyrophenone known as compound 302,089. However, glycollates such as BZ were still viewed as the most important class of chemicals. One such compound, known as EA 3834, with a faster onset time was under consideration as a replacement for BZ.<sup>40</sup> By 1969, with President Nixon's disavowal of biological weapons and reaffirmation of no first use of lethal and incapacitating chemical weapons, the US BZ weapons were officially recognised as an ineffective capability.<sup>41</sup>

Research on incapacitating agents in the UK, including close liaison with the US programme, had been underway since the late 1950's but activities had intensified in 1963 when a specific directive for the development of an offensive capability was articulated.<sup>42</sup> Dando's assessment of the UK programme in the 1960's provides some insight into the scientific limitations of research efforts during this period. Military researchers noted that the best way to develop an incapacitating agent would be to design an agent with a specific action but they observed that existing knowledge of the interactions between biochemicals and receptors was not advanced enough to make this possible. Therefore the search, as in the US, took the form of a literature search and screening of compounds with promising effects.<sup>43</sup> Efforts concentrated on those neurotransmitter-receptor systems that were better understood. Foremost amongst these was the interaction of the neurotransmitter acetylcholine with acetylcholine receptors, which were known as the site of action of the lethal nerve agents. Glycollates such as BZ also act on this neurotransmitter-receptor system. The programme investigated a variety of other compounds affecting known neurotransmitter systems including: indoles, such as LSD; tryptamines; benzimidazoles; tremorine derivatives; and morphine-like opioids such as oripavine derivatives. By the mid to late 1960's research became more systematic, with increased efforts to gain a greater understanding of the target receptors.<sup>44</sup> Research on incapacitating agents continued until at least the early 1970's but apparently no suitable agent was found, the British having not been convinced about the US Army's BZ weapon.<sup>45</sup> Doubts were expressed by UK officials over the feasibility of "nonlethal" incapacitating agents:

On general grounds I think it unlikely that ... a pure incapacitator agent will emerge. Any chemical agent, a small dose which is capable of profound disturbance of bodily of mental function, is certain to be able to cause death in large dose ... and no attack with a chemical warfare agent is likely to be designed with the primary objective of avoiding overhitting.<sup>46</sup>

Nevertheless, in the US in the early to mid 1970's new incapacitating agent weapons were moving closer to deployment.<sup>47</sup> Dissemination tests of the new glycollate agent, EA 3834, were conducted during fiscal year 1973.<sup>48</sup> In mid-1973 it was accepted for weaponization and, because of similar dissemination properties, it was envisaged that the wide variety of CS munitions could be used for delivery of the new agent.<sup>49</sup> CS was of course being used on a large scale at the time in Vietnam. Also in fiscal year 1973 the US Army approved a requirement for a tactical air-delivered incapacitating munition system (TADICAMS) and carried out advanced development of a 155mm projectile, the XM-723, and test of an incapacitating agent dispensing submunition (SUU-30/B) with EA 3834. Aside from the glycollates other types of agents under investigation at this stage were analogues of thebaine and oripavine, morphine-related compounds, and phenothiazines. Dissemination tests with the latter were carried out during fiscal year 1974.<sup>50</sup>

In 1975, with the end of the Vietnam War, military interest in incapacitants began to fade and BZ was subsequently decommissioned. As Perry Robinson has observed:

By 1976, BZ had been declared obsolete, but the agent which the Chemical Corp has selected to replace it – another glycollate, the faster action EA 3834 - was not standardized: the US military were in the process of reconsidering their requirement for such weapons.<sup>51</sup>

Some years later, between 1988 and 1990, the 90,000 lb stockpile of BZ in bulk chemical form and munitions was destroyed at Pine Bluff Arsenal in an incinerator that had been funded and constructed in the mid-1980's. As Furmanski has noted, this action was unilateral, occurring prior to bilateral discussions on chemical weapons between the US and the USSR and well before Chemical Weapons Convention (CWC) was opened for signature in 1993.<sup>52</sup>

By late 1975 increasing public interest had led to Senate hearings to examine the scope of human experimentation programmes conducted by the Department of Defence (DOD) and the Central Intelligence Agency (CIA).<sup>53</sup> Dando and Furmanski have described the extent of testing in the US Army programme:

Over the 20-year period 1956-1975 at least 6,720 soldiers and approximately 1,000 civilian patients or prisoners participated in evaluation of 254 chemical agents in at least 2,000 trials of psychochemicals.<sup>54</sup>

The Army's own assessment of the incapacitating agent programme from 1950 to 1975 concluded that \$110 million had been invested in this exploratory research. In addition to intramural research, at least 25 contracts had been awarded to external contractors including universities and hospitals, the majority of which involved testing of chemicals on human subjects.<sup>55</sup>

Despite this increasing scrutiny and decreasing military interest in an incapacitating agent capability, the Army continued with exploratory development in fiscal years 1975 and 1976, investigating a binary concept for agent dissemination, studying rocket, artillery and mortar delivery systems, and exploring the potential of benzodiazepines such as Valium as incapacitating agents.<sup>56</sup> However, one result of the Senate hearings was the introduction of greater restrictions on human testing and so in fiscal year 1977 the Army programme conducted a review of agents previously tested with a view to selecting an agent effective through inhalation and contact with the skin. One avenue under investigation was combining a glycollate with an irritant agent. Also during this period the Army conducted some advanced development including work on a pilot plant for production of the glycollate EA 3834A and a filling facility for a XM96 66mm incapacitating agent rocket warhead.<sup>57</sup> This would be the last advanced development work until the early 1990's.<sup>58</sup>

During the nine-year period from fiscal year 1978 to 1986 the incapacitating chemical program at the US Army's Edgewood Arsenal continued. However, efforts were limited to relatively low-level exploratory research into new compounds and improved delivery systems.<sup>59</sup> Nevertheless significant progress was made, as Dando has argued: "During this time there was clearly a deepening understanding of the mechanism of action of potential incapacitants, and of how they might be weaponised and used."<sup>60</sup> Several research efforts in the early to mid 1980's involved the study of

structure-activity relationships of various chemicals. By 1984 and 1985 emphasis appears to have shifted from psychomimetic compounds, such as the glycollate agents, to potent analgesics such as the opioid drug fentanyl and its analogues including carfentanil.<sup>61</sup> Fentanyl itself, which had been discovered in the late 1950's and was introduced as a clinical anaesthetic in the 1960's, had been considered as a candidate incapacitating agent as early as 1963.<sup>62</sup> However, its' analogues (or derivatives) such as carfentanil were not first synthesised until the 1970's, following a search for more potent anaesthetics with wider safety margins.<sup>63</sup> Some of these fentanyl derivatives had soon been introduced to anaesthesia practice and others were under consideration as veterinary tranquilizers.<sup>64</sup> Not long after their discovery they too were under consideration in the US Army incapacitating agent programme. The Chemical Research, Development, and Engineering Center (CRDEC)<sup>65</sup> published research into the binding properties of carfentanil at different opioid receptor sub-types, illustrating the mechanism behind its' wider safety margin.<sup>66</sup> Tests on primates in support of the programme were carried with aerosolised carfentanil during the 1980's.<sup>67</sup> Also, in fiscal year 1984 the 155mm munition containing incapacitating agent submunitions was redesigned and successfully tested. By fiscal year 1986 the search for new incapacitating agents continued drawing on academia and industry for new compounds.<sup>68</sup>

## 1.3.2 The Advanced Riot Control Agent Device (ARCAD) Programme

By 1987 the National Institute of Justice (NIJ) had established a 'Less-Than-Lethal Technology Program' following a conference in 1986 where participants had urged investigation of chemical incapacitating agents. The first research contract under this new program was an award in 1987 to the US Army's Chemical Research, Development, and Engineering Center (CRDEC) at Aberdeen Proving Ground for a feasibility assessment of a dart to deliver an incapacitating agent to stop a fleeing suspect.<sup>69</sup> After the initial study was completed the NIJ added additional funds to the research and development effort in 1989 and 1990<sup>70</sup> to identify a suitable chemical and produce a prototype delivery system.<sup>71</sup> The requirement for rapid immobilization apparently led to consideration of fentanyl analogues, in particular alfentanil, selected because of its' high potency and quick action. However, its' low safety margin was a major problem. In addition, the prototype delivery system, <sup>72</sup>

It is not clear whether these NIJ contracts for development of incapacitating agents for the police rekindled the military's own interest in these agents but in any case activity in the US Army's incapacitating agent programme increased markedly in the late 1980's and early 1990's, and the Army adopted the "less-than-lethal" terminology associated with the NIJ programme. By fiscal year 1989, under Project A554, candidate opioid chemicals had been selected and a contract awarded for estimating production costs for these agents. Unsurprisingly, given the findings of research carried out for the National Institute of Justice, the fentanyl analogues were the agents under consideration. Tests had been conducted with rodents and primates with respiratory depression a major side-effect in the latter. In an effort to militate against this danger studies had been initiated on combining such opioids with antidotes (opioid antagonist drugs) in order to increase the safety margin.<sup>73</sup>

During fiscal year 1990 the Army terminated their 'Incapacitating Chemical Program' and reinvented it as the 'Riot Control Program'. This was most likely due to the ongoing negotiation of the Chemical Weapons Convention (CWC), which would soon prohibit the development of chemical weapons. The military apparently sought to place incapacitating agents in the same category as irritant riot control agents (RCA), which the US had long maintained were not chemical weapons, an isolated position not shared by any other countries.<sup>74</sup> As Perry Robinson observed in 1994:

The chemicals themselves seem to be the same. The variant terminology reflects the changing status in international law of the weapons that are based on these chemicals.<sup>75</sup>

This attempt to soften the language in describing these weapons was not a new idea. A report from the US Defense Science Board some 30 years previously, recommending a major effort on incapacitating agent development during the 1960's, had put forward new terminology to avoid political restrictions and public opposition:

It was argued that the ideal incapacitating agent should not be classed with the toxic biological or chemical agents and that it should be characterized by some new term, such as *'reinforced tear gas'*, or *'super tear gas'*, to emphasize its relatively innocuous nature.<sup>76</sup> [emphasis added]

Thirty years later, in 1990, incapacitating agents were being described as "Advanced Riot Control Agents". During fiscal year 1990 further development work included evaluating candidate compounds, carrying out inhalation tests, investigating dissemination techniques, and developing production methods.<sup>77</sup> An 'Acquisition Plan' for obtaining a chemical incapacitant weapon was approved by mid-1991. The Advanced Riot Control Agent Device (ARCAD) was described as follows in the US Army's *NBC Modernization Plan* in 1992:

The ARCAD consists of a hand held grenade, or device, that can also be shoulder fired from a weapon currently being used or developed. This device will deliver a potent riot control compound, which will provide a rapid onset of effects where the safety of the individual(s) is the primary concern. The candidate compound will be effective primarily through the respiratory tract.<sup>78</sup>

By fiscal year 1993 the ARCAD had entered advanced development under Project DE78, with \$10.2 million funding for the year. Further work was conducted on the delivery system with a plan for testing and evaluation updated and a preliminary plan for manufacture of the ARCAD completed.<sup>79</sup> A contract for development of the ARCAD was scheduled to be awarded by late 1993 and planned work for fiscal year 1994 included initiating the prototype design and hardware fabrication.<sup>80</sup> It seems that a decision was taken at some point during this period that the ARCAD would not move forward into the Department of Defense's (DOD) major systems development process.<sup>81</sup> This was due to the provisions of the Chemical Weapons Convention (CWC), which opened for signature in January 1993, prohibiting chemical weapons and limiting the use of riot control agents to "law enforcement including domestic riot control purposes".<sup>82</sup> The US military had of course already sought to characterise these incapacitating chemical weapons as riot control agents despite them being centrally acting incapacitating agents rather than peripherally acting irritant agents.

Even though the advanced development of the ARCAD weapon had been curtailed, the search for new agents continued. Researchers at Edgewood Research, Development, and Engineering Center (ERDEC) had carried out considerable work on fentanyl analogues, from which compounds had been selected for the ARCAD.<sup>83</sup> However, the limitations of these compounds had fuelled the search for new compounds. As a DOD solicitation for research proposals on 'Less-Than-Lethal Immobilizing Chemicals' in late 1992 concluded:

Most recent less-than-lethal (LTL) programs at US ARMY ERDEC focused on the fentanyls as candidate compounds. ... Many of these compounds are well-characterized, rapid acting, very potent and reliable in their activity. However, for many LTL applications, they have safety ratios that are too low and durations of action that are too long. Ideally one needs a material that will act safely, virtually instantaneously and last for just a few minutes. Thus, candidate chemical immobilizers with improved safety ratios and shorter duration of action are needed.<sup>84</sup>

Within the ERDEC research laboratories attention had turned to a class of sedative compounds called the alpha<sub>2</sub> adrenergic agonists, which were subsequently found to cause sedation by binding to alpha<sub>2</sub> adrenergic receptors in the locus coeruleus area of the brain.<sup>85</sup> A multidisciplinary study of these compounds had been initiated at ERDEC in 1989.<sup>86</sup> Further research was carried out at Edgewood in the early 1990's with particular attention to a drug called medetomidine, which had been introduced as a sedative and analgesic for veterinary practice in 1989.<sup>87</sup> Work focused on modifying medetomidine to produce more selective analogues with potent sedative properties but without the cardiovascular side effects that medetomidine causes, namely low blood pressure.<sup>88</sup> By 1994 Army researchers were putting their faith in alpha<sub>2</sub> adrenergic agents as future incapacitating chemical weapons:

More selective  $\alpha_2$ -adrenergic compounds with potent sedative activity have been considered to be ideal next generation anesthetic agents which can be developed and used in the Less-Than-Lethal Technology Program. Unlike opioids, these compounds are devoid of the usual liabilities associated with respiratory depression, physical dependence and environmental concern after dissemination...<sup>89</sup>

In April 1994 Technical Directors at ERDEC argued that the Advanced Riot Control Agent (ARCAD) Program should be revived, putting forward proposals for research on incapacitating agents.<sup>90</sup> A three-year, \$1.25 million Advanced Concept Technology Demonstration (ACTD)<sup>II</sup> effort entitled *Demonstration of Chemical Immobilizers* was proposed, defining these agents as:

...chemical compounds that produce incapacitation through immobilization, disorientation or unconsciousness. Among the classes of neuropharmacologic agents with potential as immobilizers are anesthetics, analgesics, sedatives and hypnotics.<sup>91</sup>

The stated objective of the research was: "Select, acquire and demonstrate the effectiveness and safety of a chemical immobilizer(s) on test animals, such as rodents and primates", focussing on agent delivery through inhalation and also carrying out limited tests of a prototype delivery system. The proposed research would comprise Phase 1 of a longer four phase programme, the latter phases envisaged as follows: Phase 2 – Expanded toxicological testing; Phase 3 – Delivery system development, and Phase 4 – clinical trials for effectiveness and safety. For Phase 1 the proposal

<sup>&</sup>lt;sup>II</sup> The US Department of Defense defines Advanced Concept Technology Demonstrations (ACTDs) as programmes to "...exploit mature and maturing technologies to solve important military problems." See Department of Defense web site, available March 2007 at: <u>http://www.acq.osd.mil/actd/intro.htm</u>

advocated a generic approach called 'Front End Analysis' to select the most suitable chemical compounds for the envisioned scenarios based on prior ERDEC research and knowledge of these agents. Furthermore the author suggested that concurrent studies be conducted on two classes of compound likely to be selected in the Front End Analysis, namely synthetic opioid anaesthetics and alpha<sub>2</sub> adrenergic sedatives.<sup>92</sup>

These two lines of research were expanded in the supporting research proposals, also dated April 1994, authored by Edgewood Researcher C. Parker Ferguson, entitled *Antipersonnel Chemical Immobilizers: Synthetic Opioids*<sup>93</sup> and *Antipersonnel Chemical Immobilizers: Sedatives.*<sup>94</sup> With regard to opioids the proposal noted that the major side effect of respiratory depression could be countered, and the safety margin increased, by combining the agent with an antidote:

Previous studies under the Advanced Riot Control Agent Device (ARCAD) program led to materials with dramatically improved safety ratios. This was achieved by mixing a fentanyl agonist with an antagonist that blocks the respiratory depression.<sup>95</sup>

A patent illustrating just this strategy was filed by ERDEC in December 1994 claiming a novel combination of fentanyl derivative agonist and antagonist that induces analgesia, sedation, and anaesthesia with minimal respiratory depression. The patent notes that various derivatives could be used but that sufentanil was preferable. Furthermore the patent noted that "...the development of opiate drugs to create a drug that causes analgesia without respiratory depression has been an elusive goal..." despite the emergence of more selective agents.<sup>96</sup>

The proposal for development of opioid incapacitating agents also referred to new fentanyl analogues with shorter durations of action, patented by Glaxo Pharmaceuticals in the early 1990's. Although not mentioned in the proposal, one of these was remifentanil, since approved for use in anaesthesia.<sup>97</sup> Clearly at this point fentanyl analogues remained the prime candidates for the Army's incapacitating agent programme, as the proposal noted: "Extensive studies have been carried out in the past and the most advanced technology exists for the fentanyls than for any other chemical immobilizer candidates."<sup>98</sup> The proposal also gives an indication of the dual use nature of advances in the development of analgesics and anaesthetics in the pharmaceutical industry. The author notes that Glaxo's short acting fentanyls had only undergone preliminary evaluation at ERDEC but that the results of clinical trials underway in industry would assist in the evaluation of these compounds as incapacitating weapons agents.<sup>99</sup>

The proposal relating to sedative compounds envisioned initial studies to design and synthesize new alpha<sub>2</sub> adrenergic compounds:

Conduct Structure Activity Relationship (SAR) studies to determine a basic pharmacophore<sup>III</sup> and to design and synthesize new alpha2-adrenergic agonists that cause immobilization by profound sedation. Emphasis will be on synthesis of quicker and shorter acting safer materials than those that currently exist; starting point for synthesis will be on newly designed compounds based on previous molecular modelling and SAR studies conducted at ERDEC.<sup>100</sup>

Subsequently selected compounds would proceed to in vitro and animal testing. The proposal noted the aforementioned cardiovascular side effects and the slow onset

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 $<sup>^{\</sup>rm III}$  Defined as the molecular basis of a drug's activity at receptor sites.

times of previously tested compounds. Interestingly, it also acknowledged some of the practical limitations that apply to any incapacitating chemical agent:

Operational limitations include the potential use in mixed populations of the very young, the elderly, those in poor health and those who may react adversely to a specific chemical.<sup>101</sup>

In addition to the proposed work on fentanyl derivatives and alpha<sub>2</sub> adrenergic agonists as "chemical immobilizers", researchers at Edgewood proposed a modest feasibility study of other potential incapacitants, which they termed "calmative agents" and defined separately:

A calmative agent can be defined as an antipersonnel chemical that leaves the victim awake and mobile but without the will or ability to meet military objectives or carry out criminal activity.<sup>102</sup>

Clearly the author of this April 1994 proposal, also C. Parker Ferguson, viewed "calmatives" as distinct from "immobilizing agents" in view of their mechanism of action not involving anaesthesia or sedation, it being more akin to the focus of early cold war efforts on psychomimetic action.<sup>103</sup> As detailed in the document, the impetus for this research proposal on "calmatives" arose from observations of a Professor of Anaesthesiology at the University of Utah School of Medicine, Prof. Theodore Stanley. He had passed on his observations of the effects of an experimental serotonin antagonist or blocker, which he had found to have a "profound claming effect" on wild elk. The proposed feasibility study envisaged a literature search to determine the structure of serotonin (5-HT) antagonists acting on serotonin receptors in order to find the subtypes responsible for different pharmacological effects. Researchers would also seek to collaborate with outside experts in further investigating these agents as weapons:

Identify and interact with expert(s) in academe, other government agency (OGA) or pharmaceutical laboratories to help identify or design compound(s) for desired effect.  $^{104}$ 

Prof. Stanley, who had been pioneering novel oral (trans-mucosal) fentanyl delivery systems for pain management during the 1990's, is an international expert on anaesthetic and sedative drugs, and drug delivery.<sup>105</sup>

Although there is insufficient information to reach a concrete conclusion, the proposed research efforts do not appear to have been accepted at the time. In late 1995 the author of the proposals, C. Parker Ferguson, presented a paper to the ERDEC annual Scientific Conference on Chemical and Biological Defense Research on the 40-year history of incapacitating agent research at the US Army's Edgewood Arsenal. The abstract of this paper gives an overview of the types of compound under consideration and the types of scenario envisaged for their application at this point in time:

Among the most mature of Less-Than-Lethal technologies are antipersonnel chemicals that render an adversary incapable of carrying out a military mission or criminal activity without permanent harm to people or property. Potential military missions include peacekeeping operations; crowd control; embassy protection; and counterterrorism. Law enforcement applications include use by local, state and national law enforcement agencies in hostage and barricade situations; crowd control; close proximity encounters; prison riots; and to halt fleeing suspects. Depending on the specific scenario, several classes of chemical have potential use, to include: potent analgesics/anesthetics as rapid acting immobilizers; sedatives as immobilizers; and calmatives that leave the subject awake and mobile but without the will or ability to meet objectives. $^{106}$ 

The National Institute of Justice (NIJ) had also continued to fund research into incapacitating agents and delivery systems during the 1990's. Following on from the research carried out on their behalf at the US Army's Edgewood Research, Development and Engineering Center (ERDEC) in 1989 and 1990, NIJ initiated a project with Lawrence Livermore National Laboratory (LLNL) in late 1992 that continued to assess the feasibility of using fentanyl derivatives, with consideration of combining them with antidotes to enhance the safety margin, and solvents to enable delivery through the skin.<sup>107</sup> Initial work focused on alfentanil but by late 1993 attention had shifted to another analogue, lofentanil, because of its higher safety margin.<sup>108</sup> Research at the Forensic Science Center at LLNL continued until at least January 1997, when a final report, including recommendations for further NIJ-sponsored work, was issued. This report is entitled *Dose Safety Margin Enhancement for Chemical Incapacitation and Less-Than-Lethal Targeting*, and gives an insight into the agent selection process and technical approach to agent delivery.<sup>109</sup>

As with prior military efforts, a major theme of the LLNL research was to investigate the possibility of using anaesthetic compounds in combination with antidotes to widen the safety margin for potent chemical incapacitating agents. Further objectives of the research were set out in the introduction to the report:

We were requested to investigate and compare the efficacy of the most potent pharmaceutical agents currently available that could incapacitate an individual. We were to perform a literature review and compare all of the potential less-than-lethal pharmaceutical agents. Finally, we were asked to recommend future research concerning less-than-lethal delivery systems.<sup>110</sup>

The major difference between this NIJ sponsored effort and military research was the stated objective to develop a weapon for use against an individual as opposed to a munition (grenade, mortar, or artillery) for wide area delivery. However the researchers were also tasked with considering scenarios beyond law enforcement needs including military special operations and low intensity conflict.<sup>111</sup>

Their initial literature review considered anaesthetics in clinical use to compare the doses required, onset time, and side effects. A summary of their findings is shown in Table 2 below.

Drug class	Example	Clinical Dose (IV)	Onset Time (IV)	Side Effects
Barbiturates	Sodium thiopental	200-500 mg	10-20 secs	Respiratory depression, hypotension
Benzodiazepines	Diazepam (Valium)	25 mg	1-2 mins	Some cardio- pulmonary depression
Opioids	Morphine Meperidine Fentanyl	1-2 mg (analgesic) 10-25 mg (analgesic) 0.05-0.1 mg (analgesic)	Not given Not given Seconds	Respiratory depression
Neuroleptic- opioid combinations	Butyrophenone (Droperidol) & fentanyl mixture (Innovar)	0.1ml/kg Innovar (2.5mg Droperidol & 0.05 mg Fentanyl)	Not given	Respiratory depression, nausea and vomiting

**Table 2:** Lawrence Livermore National Laboratory (LLNL) literature review of clinical anaesthetics.<sup>112</sup>

The LLNL literature review covered only clinical anaesthetic agents delivered intravenously. Inhalation anaesthetics were not considered due to the lack of dose control that would be possible in field conditions, a view clearly not shared by military developers. All the agents were found to have significant side effects, in particular respiratory depression. As regards onset times, benzodiazepines were found to act relatively slowly due to limited passage through the blood brain barrier and were required to be delivered intravenously for maximum effect. Whilst the barbiturate sodium thiopental was found to have a rapid onset time, since it crosses the blood-brain barrier quickly, it would also need to be delivered intravenously. The most notable difference between the drugs considered by the researchers was the potency and therefore dose required which led to the selection of fentanyl and analogues for the next stage of the literature review:

... it became apparent that fentanyl (Janssen Pharmaceuticals) is an uncommon and very powerful drug. Whereas other compounds, such as sodium pentothal, benzodiazepines, and morphine elicit an anesthetic response at dosage levels of 3-200mg, fentanyl is highly effective in humans at microgram levels.<sup>113</sup>

Moreover fentanyl and its analogues, from the piperidinyl family of opioids, were observed to be extremely fast acting, crossing the blood-brain barrier very quickly due to their lipophilic properties. They noted that, in addition to greater potency and hence lower effective doses, these compounds also had better safety margins than morphine. They concluded, unsurprisingly in the light of prior military and NIJ-sponsored research on these agents, that "all pharmacologic and pharmacokinetic parameters point to this class of drugs [fentanyl and analogues] as an ideal candidate for less-than-lethal technology."<sup>114</sup>

The report also describes work carried out by LLNL researchers on a delivery system for these types of chemical agent. Having discounted delivery by inhalation due to the lack of control in administering the agent in the field,<sup>115</sup> and been asked by the NIJ not to consider injecting delivery systems, such as darts or syringes, the researchers turned to alternative methods of drug delivery.<sup>116</sup> They drew their inspiration from drug skin patches, for example nicotine patches for nicotine withdrawal, and fentanyl patches for severe burns, where the drug is combined with a solvent for delivery

through the skin (transdermal). The researchers chose dimethylsufoxide (DMSO) as the solvent, noting:

The main advantage of a solvent/drug delivery system is that the anesthetic drug formulation need only pass through the epidermis layer of the skin to reach the blood vessels.<sup>117</sup>

Subsequently they tested a delivery system concept comprising a felt pad soaked with DMSO and fired from an air rifle. They found that a drug/DMSO mixture could be delivered in this way and that the material would penetrate thin clothing but thick clothing would be a sufficient countermeasure. They considered that the delivery system would have to be encapsulated to enable practical use and carried out tests using a 38-calibre cartridge to deliver the felt pad, achieving similar results to the airgun tests. However they proposed that future developments should consider smaller fully encapsulated 'paintball' type projectiles containing the drug and solvent mixture.<sup>118</sup>

The report also considered the issue of mixing antidotes with the fentanyl-type drugs in order to increase the safety margin, noting that the antidote of choice for opioid toxicity is naloxone, an opioid antagonist which acts quickly (minutes) and for a long duration (hours) to reverse the respiratory depression, low blood pressure, and sedative side-effects of opioids. Since simply mixing naloxone with the opioid anaesthetic would defeat its' effects the researchers observed: "...it appears desirable to utilize a timed-release combination of naloxone with an ultrafast-acting fentanyl based-anesthetic formulation"<sup>119</sup> [their emphasis]. From their initial investigations and consultations with a private company they proposed that the naloxone could be delivered within a 'caged structure' of cyclodextrin molecules enabling delayed release. They noted that the major research issue would be developing the slow release mechanism for the naloxone-cyclodextrin structure so that it reached maximum effect only after the anaesthetic drug had sufficient time to act.<sup>120</sup> Their consultations with the private company apparently led to a suggestion for a new delivery mechanism:

Meetings with Fuisz Technologies also produced another idea for placing a fentanylbased/antidote system within a cyclodextrin 10-micron powder. The dry powder could be dispersed as a smoke during a hostage situation. Terrorists would be incapacitated by breathing anesthetic smoke injected into an air duct or office building air conditioning system.<sup>121</sup>

In terms of further work the researchers argued that *in vitro* tests of the drug/solvent soaked felt projectiles on animal and human cadaver skin to measure the passage of the mixture through the skin and the effect of the projectile on absorption should be the next step in the development of the weapon, followed by extensive animal testing with various fentanyl derivative – DMSO mixtures.<sup>122</sup> Subsequently, they proposed, human tests with volunteers should be conducted in co-operation with a university medical centre and concluded that a final weapon system could be produced in 2-5 years depending on the level of funding and number of institutions involved.<sup>123</sup> It is unclear whether follow-on work was conducted but the US Army would later return to this concept of a fentanyl-DMSO felt projectile.

## **1.4 Contemporary Programmes**

## 1.4.1 Agents

## United States

With the founding of the Joint Non-Lethal Weapons Program (JNLWP) in July 1996 and the subsequent establishment of the Joint Non-Lethal Weapons Directorate (JNLWD) as its' institutional base, research and development of "non-lethal" weapons gained renewed impetus. A preliminary legal review of proposed chemical "non-lethal" weapons, carried out by Navy lawyers (in the Judge Advocate General's office) at the request of the JNLWD and published in November 1997, seemingly provided the legal ambiguity necessary for US military research on chemical incapacitating agents and delivery systems to proceed, despite the entering into force of the Chemical Weapons Convention (CWC).<sup>124</sup>

The first indication of a new research program on chemical incapacitating agents emerged in December 1999. Following discussions with the JNLWD the US Army issued a solicitation under its' Small Business Innovation Research programme for fiscal year 2000 that included a request for proposals on "Topic# CBD 00-108: Chemical Immobilizing Agents for Non-lethal Applications." The objective of the required research was to develop new chemical incapacitating agents for military and law enforcement purposed based upon recent technological advances:

Previously developed or proposed incapacitating or immobilizing agents have been deficient in one or more technical aspects. These deficiencies include low safety ratios and inadequate performance characteristics, such as, reliability of desired response, onset time to effects and duration of effects. *Recent pharmaceutical developments suggest that new approaches to safer chemical immobilizers with improved performance characteristics may be available*.<sup>125</sup> [emphasis added]

The solicitation detailed the planned research, which would consist of a three-phase effort. Phase I would seek to identify new agents and agent combinations including an analysis of "…recent breakthroughs in the pharmacological classes such as Anesthetics/analgesics, tranquilizers, hypnotics and neuromuscular blockers" and subsequently:

Design and conduct a toxicological test program with these new immobilizing agents to fill data gaps. Establish the mode of immobilization, the effective dose(age) for immobilization, onset time and duration of effects, and safety ratio in the most appropriate animal species. Correlate these new experimental results with existing data, if any, from other studies, especially in humans (clinical tests) and non-human primates to establish feasibility of use for non-lethal applications.<sup>126</sup>

This research, it was envisaged, would be followed by Phase II of the project where input from various military and law enforcement agencies would be gathered in order to establish the required characteristics of chemical agents for potential scenarios of use, the implications of the CWC on those scenarios then being assessed. Following the selection of the preferred scenarios, tests would be conducted on non-human primates followed by clinical tests on humans to assess safety and operational characteristics. Furthermore an appropriate delivery system would be designed and demonstrated. The final part of the project, Phase III, would consider the dual use applications of the technology. Potential military uses given in the solicitation were "meeting US and NATO objectives in peacekeeping missions; crowd control; embassy protection; rescue missions; and counter-terrorism" whereas law enforcement applications cited were "hostage and barricade situations; crowd control; close proximity encounters, such as, domestic disturbances, bar fights and stopped motorists; to halt fleeing felons; and prison riots."<sup>127</sup>

The closing date for this solicitation was 12 January 2000. In March 2000 the US Army Soldier and Biological Chemical Command (SBCCOM) announced that a proposal had been selected for funding by Edgewood Chemical Biological Center (ECBC), formerly Edgewood Research, Development, and Engineering Center (ERDEC).<sup>128</sup> By June 2000 ECBC had awarded the contract for Phase I of the research to a company called OptiMetrics, Inc.<sup>129</sup> The principal researcher for the project would be C. Parker Ferguson, who had worked at ECBC previously, and had been the author of the 1994 Edgewood proposals for research and development of "immobilizing agents" and "calmatives". He had also presented a paper on chemical "immobilizing agents" to the *Non-Lethal Defense IV conference*, which was held in March 2000, and co-sponsored by the Joint Non-Lethal Weapons Directorate (JNLWD), Army Research Laboratory (ARL), National Institute of Justice (NIJ), and Oak Ridge National Laboratory (ORNL). The award announcement summarised the direction of the Phase I research:

*Recent studies suggest three new agent combinations with potential for meeting user objectives.* Phase I studies will consist of a Front End Analysis comprising the following elements: review existing data on the candidate agents; define scenarios of use and operational parameters; conduct range finding toxicological animal tests, and correlate results with those from previous studies. The purpose of the FEA is to determine feasibility for one or more candidates as immobilizing agents. <sup>130</sup> [emphasis added]

Unsurprisingly the description of the research, including the 'Front End Analysis' methodology, paralleled the 1994 ERDEC proposals. According to an employee of OptiMetrics, speaking in 2004, the contract award was \$75,000<sup>131</sup>, and the research concentrated on fentanyl analogue – antidote mixtures.<sup>132</sup> It is not clear when this Phase I research was completed but it was carried out by November 2002 at the very latest. Neither is it apparent when or if the Phase II and Phase III research was conducted and, if so, whether it was carried out 'in house' or on contract.<sup>133</sup>

A related part of US research into incapacitating chemical weapons at this time was a literature search and analysis carried out jointly by the Applied Research Laboratory (ARL) and the College of Medicine at Pennsylvania State University (PSU). The ARL is where the JNLWD-sponsored Institute for Non-Lethal Defense Technologies (INLDT) is located, itself run by a former director of the JNLWD. Furthermore the ARL is a Department of Defense designated research centre for the Navy and, since 1999, has been the designated Marine Corps Research University (MCRU). On the 3<sup>rd</sup> October 2000 the ARL published the results of their literature search in a document entitled *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*.<sup>134</sup>

The introduction to the report set out the objectives of the research project, which emphasised advances in science and technology:

- Define the advantages and limitations of pharmaceutical compounds as calmatives with potential use in non-lethal techniques.
- Provide a comprehensive survey of the medical literature utilizing pharmaceutical agents to produce a calm state with potential for use as a non-lethal technique. This information will provide a current database of the relevant literature on calmatives.
- Provide an in-depth review of selected calmatives identified by the literature search with high potential for further consideration as a non-lethal technique.
- *Identify and recommend promising new areas in pharmaceutical drug development that are poised to uniquely meet the requirements of calmatives as non-lethal techniques.*<sup>135</sup> [emphasis added]

In the report, the researchers define "calmatives" as "...compounds known to depress or inhibit the function of the central nervous system termed (depressants)", including "...sedative-hypnotic agents, anesthetic agents, skeletal muscle relaxants, opioid analgesics, anxiolytics, antipsychotics, antidepressants and selected drugs of abuse."<sup>136</sup> In contrast to ECBC researchers, who distinguished between so called "immobilizing agents" and so called "calmatives", this study groups all potential incapacitating agents including potent anaesthetic chemicals as "calmatives". This softening of language in describing these chemical weapons is a feature of the report and reflects wider efforts to present new weaponry as 'techniques' or 'capabilities',<sup>137</sup> and indeed prior efforts to describe incapacitating agents as "advanced riot control agents". Nowhere in the report is the word 'weapon' used, the authors preferring to use the phrase "non-lethal technique".

The authors set out what they see as the ideal characteristics of incapacitating chemical weapons for the military and police, what they refer to as "calmatives":<sup>138</sup>

- Easy to administer via various routes i.e. transdermal, intramuscular, inhalation etc.
- Rapid onset (seconds)
- Short duration of action (minutes)
- Comparable effects on individuals of similar body weight and age
- Reversible effects by rapid metabolism or selective antagonist (antidote)
- Safe for end-user to deliver
- No prolonged toxicity to the victim
- Side-effects of short duration

The report suggests that different chemical agents would be required for different scenarios with "...different mechanisms of action, duration of effects and *different depths of "calm"*."<sup>139</sup> The latter phrase is bizarrely obfuscating in that it essentially means they are considering effects ranging from a reduction of anxiety to anaesthetically induced unconsciousness. They illustrate this by describing two differing practical scenarios:

For example, an individual running towards you with a gun may pose an immediate threat or perhaps be trying to protect you; in contrast with this immediate threat are a group of hungry refugees that are excited over the distribution of food and unwilling to wait patiently. In these two cases the degree of "calm" required is vastly different in magnitude and the target populations are also different.<sup>140</sup>

Although the report doesn't consider delivery systems *per se* the authors envisage a variety of delivery routes including "...application to drinking water, topical

administration to the skin, an aerosol spray inhalation route, or a drug filled rubber bullet...". $^{141}$ 

In their literature search the researchers analysed both pre-clinical and clinical medical research to yield information about dose-response effects and cellular mechanisms of action (pre-clinical) as well as behavioural effects, effective doses, routes of administration, and toxicity (clinical).<sup>142</sup> Their analysis of the available literature identified several classes of drug which they considered to have "high potential". These, along with their receptor sites of action are listed in Table 3 below.

Drug Class	Examples	Site of Action	
Benzodiazepines	Diazepam, midazolam,	GABA receptors	
	eitzolam		
Alpha <sub>2</sub> Adrenergic Receptor	Dexmedetomidine	Alpha <sub>2</sub> -adrenergic receptors	
Agonists			
Dopamine D3 Receptor	Pramipexole, Cl-1007	D3 receptors	
Agonists			
Selective Serotonin Reuptake	Fluoextine, WO-09500194	5-HT transporter	
Inhibitors			
Serotonin 5-HT <sub>1A</sub> Receptor	Busprione, lesopitron	$5-HT_{1A}$ receptor	
Agonists			
Opioid Receptors and Mu	Carfentanil	Mu opioid receptors	
Agonists			
Neurolept Anesthetics	Propofol	GABA receptors	
Corticotrophin-Releasing	CP 154,526, NBI 27914	CRF receptor	
Factor Receptor Antagonists			
Cholecystokinin B receptor	Cl-988, Cl-1015	CCKB receptor	
antagonists			

 Table 3: Selected calmatives.<sup>143</sup>

Unsurprisingly, the Pennsylvania State study draws attention to a number of classes of drugs that have long been considered as potential incapacitating agents including opioids, benzodiazepines, alpha<sub>2</sub> adrenergic agonists, and neurolept anaesthetics. With regard to opioid drugs, the report focuses on one fentanyl analogue in particular, carfentanil. The authors note that carfentanil has long been used to immobilize large animals but has not been used in humans and cite its' ease of delivery as a particular advantage:<sup>144</sup>

Carfentanil has been administered intramuscularly via dart injection, intravenously, and orally. Therefore, this drug offers the distinct offers the distinct advantage of being administered to subjects at far distances.<sup>145</sup>

The additional advantage of the availability of naloxone as an antidote to this and other opioid drugs is also noted. Their discussion of opioid receptor function points out that the powerful analgesic properties of opioids such as fentanyl analogues are produced by action on the  $\mu$  sub-type of opioid receptors. Furthermore they note the analgesic properties are caused by binding to  $\mu_1$  receptors whilst the major side effect of respiratory depression is associated with the other subtype,  $\mu_2$  receptors. It follows that an opioid drug with selectivity for  $\mu_1$  over  $\mu_2$  receptors would be attractive as an incapacitating agent because of an increased safety margin. This is something that researchers at the US Army's Edgewood Research, Development and Engineering Center (ERDEC) were pursuing during the 1980's, publishing research that found carfentanil had a greater selectivity for  $\mu_1$  receptors than  $\mu_2$  receptors, thus resulting in lower respiratory depression than some other compounds with less selectivity.<sup>146</sup>

The reports' analysis of benzodiazepines also reviews them favourably as potential incapacitating agents:

Benzodiazepines are prototypical calmative agents with varying profiles from rapid onset and short acting, through intermediate acting, to very long term effects. The agents can be administered by a variety of routes, including oral and parenteral (intramuscular an intravenous). ... This literature search had indicated that benzodiazepines (and all GABA receptor agonists) have a major potential use as non-lethal technique calmatives.<sup>147</sup>

Benzodiazepines exert their effects through action at GABA<sub>A</sub> receptors, causing sedation but also the side effects of respiratory and cardiovascular depression. An antagonist drug, flumenzenil, can be used as an antidote. The Pennsylvania State researchers highlight two areas of interest with regard this class of drug as an incapacitating agent. The first is the development of new short acting compounds that have a rapid onset of effect with a short duration (minutes). An existing short acting compound midazolam is described as: "...useful for sedation and anesthetic induction, processes which may occur in as little as two to five minutes following intravenous injection."<sup>148</sup> The report notes that newer short acting compounds are under investigation including eitizolam and Ro 48-6791. The other area of research discussed is that relating to the function of GABA<sub>A</sub> receptors. It appears that particular effects are mediated by different combinations of GABA<sub>A</sub> receptor subunits and the researchers suggest this may enable the development of sedative drugs without side effects:

With  $GABA_A$  receptor subunits expressed differentially in various brain regions, it may be possible to design benzodiazepines that mediate sedative or anxiolytic effects without causing respiratory and cardiovascular depression.<sup>149</sup>

Alpha<sub>2</sub> adrenergic agonist drugs, which had been singled out as candidate incapacitating agents some years previously by US Army researchers, are also considered. The report focuses on dexmedetomidine (Precedex), the stereoisomer of medetomidine initially developed as a veterinary drug and first approved for use in humans as recently as 1999, which causes sedation through highly selective action on the alpha<sub>2A</sub> receptor subtype over the alpha<sub>1</sub> subtype which causes low blood pressure.<sup>150</sup> The Pennsylvania State report highlights its' synergistic action with other drugs:

Used in conjunction with most other sedative agents, this drug markedly (23-90%) reduces the dose requirements for the primary agent, often reducing side effects leading to increased safety of the mixture of pharmaceutical agents.<sup>151</sup>

Furthermore the report notes that dexmedetomidine attenuates the side effects of ketamine, it can be delivered via several routes (intravenous, intramuscular, and transdermal), and it accentuates the effects of electrical currents on the body.<sup>152</sup> They note the ongoing development of a selective antagonist (antidote) called fluparoxan that they argue would: "… permit the rapid reversibility of drug-induced effects and enhance the safety profile of alpha2 adrenoreceptor agonists as non-lethal calmative techniques."<sup>153</sup>

In the reports' discussion of neurolept anaesthetics, propofol is given as an example of an agent that causes rapid anaesthesia through inhibiting nerve transmission at GABA receptors and requires no antidote due to rapid metabolism. Again the authors note the synergistic properties. Clinically propofol is used with other GABA acting agents, such as the benzodiazepine midazolam, to decrease the dose requirements and safety margin of both agents. The report emphasises that this is an area warranting further research:

The clinical experience of using multiple GABA stimulating agents as well as other synergistic drugs will be directly transferable, as new drugs in all these classes become available.

This topic is recommended for further research and holds great promise for non-lethal applications...  $^{154}\,$ 

Like the Lawrence Livermore researchers several years earlier, the report also addresses neurolept anaesthetic combinations, including the combination of droperidol and fentanyl, which produces a neuroleptic state "…characterized by marked tranquilization and sedation with a state of mental detachment and indifference while reflexes remain essentially intact."<sup>155</sup> The authors note that droperidol itself has too long a duration of action to be considered as an incapacitating agent and has significant side effects but that further research should be carried out on drugs inducing this neuroleptic state. Pointing out that droperidol acts on a number of different receptors they argue that a mixture of selective drugs acting on specific receptors could be developed to "…reproduce the neuroleptic state without the undesirable side effects."<sup>156</sup>

In addition to the drug classes described above, that had commonly been considered as potential incapacitating agents in the past, the Pennsylvania State report also puts forward the case for consideration of a number of other classes of agent based on new developments in the pharmaceutical industry. The authors argue that dopamine D3 receptor agonists, in use for treatment of Parkinson's disease and under investigation for treatment of schizophrenia, are of great interest as incapacitating agents due to their anti-psychotic properties and effects on motivation and locomotion. However, they note that the role of the D3 receptor is generally unknown and that more experimentation would be needed in order to elucidate the mechanism of action for the antipsychotic effects of these drugs.<sup>157</sup>

The report draws attention to drugs affecting serotonin (5-HT) receptors. In a discussion of selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac) and sertraline (Zoloft), which are used to treat depression and anxiety, the report also notes their effect on sleep (i.e. increased drowsiness) and on reducing aggression. Although such drugs commonly have a very slow onset time (one week or more) for effects on mood, the report argues that it is likely that an SSRI with a rapid rate of onset can be identified especially given the ongoing intensive development of these types of drugs in the pharmaceutical industry.<sup>158</sup> Drugs that bind selectively to activate a particular serotonin receptor subtype, the 5-HT<sub>1A</sub> receptor, are also considered due to their effects in reducing anxiety and aggression. Buspirone is given as the primary example of a serotonin 5-HT<sub>1A</sub> receptor agonist, which the authors recommend for consideration as an incapacitant, noting "The use of a selective 5-HT<sub>1A</sub> receptor agonist would reduce symptoms of anxiety in an

individual and promote a calmer and more compliant behavioral state."<sup>159</sup> The report points out that the onset of effect is slow and suggests that such an agent may be useful for particular situations:

Use of a transdermal patch to deliver buspirone may be effective in a prison setting where there may have been a recent anxiety-provoking incident or confrontation and this application warrants further consideration as a specific type of non-lethal technique.<sup>160</sup>

The authors also note the ongoing development of more potent drugs in this class such as lesopitron, MCK-242, and alnespirone.<sup>161</sup>

Furthermore, the report addresses the bioregulatory peptide corticotrophin-releasing factor (CRF), whose action at CRF receptors in the central nervous system is linked to mood and stress. It observes that a novel approach may be the use of CRF receptor antagonist peptides (or synthetic analogues) to produce "a calm behavioral state", noting that improved delivery mechanisms for peptides would be required.<sup>162</sup> Another peptide system considered is that of cholecystokinin (CCK). Various CCK peptides act on CCK-A and CCK-B receptors in the brain with the latter receptors involved in anxiety and panic attacks. The report notes that CCK-B agonists have been shown to induce panic attacks, whereas CCK-B antagonists appear to inhibit panic and produce a calmer state.. Therefore, the authors suggest that CCK-B antagonists, such as Cl-988 and Cl-1015, should be considered as potential incapacitating agents:<sup>163</sup>

Taken together, *recent biomedical advances* suggest that not only does a new class of calming agents, CCK-B receptor antagonists, need to be explored further, but also, appropriate delivery methods for getting these compounds to their sites of action must also be considered.<sup>164</sup> [emphasis added]

Overall the report favours the development of new incapacitating biochemical weapons, arguing that there are a wide variety of drug classes and specific agents that may be considered as potential weapons. The recommendations section notes ongoing work on new delivery mechanisms: "Several innovative approaches are under investigation for improving drug delivery via oral, pulmonary, subcutaneous and transdermal routes".<sup>165</sup> It also emphasises the synergistic action of some drugs used together to produce greater and different effects to those produced when the agents are used alone, noting that combining agents may be advantageous in the design of new incapacitating biochemical weapons and that examples of new synergistic combinations are emerging from anaesthesia practice.<sup>166</sup> The authors recommend that further research be carried out to assess the pharmacological profiles of the agents highlighted in the report as well research to identify the most effective routes for drug delivery. They also recommend collaboration with the pharmaceutical industry in the identification and development of new incapacitating chemical weapons. A final recommendation is that a similar study be conducted to assess the potential of two other major groups of pharmaceutical agents: drugs of abuse (including selected club drugs) and convulsants.<sup>167</sup>

In summarising their literature review and the contribution of their report the ARL authors point out that there are numerous drugs in clinical practice that are candidate incapacitating agents and that a wide range of compounds are under investigation in

the pharmaceutical industry for their ability to induce the types of sedative and behavioural effects of interest. Furthermore they note that:

...the goals of new drug development efforts, namely continued improvement in specificity, selectivity, safety and reversibility are the goals for improvements in non-lethal techniques.<sup>168</sup>

Concluding: "The extensive survey of the literature conducted on calmatives serves to emphasize that the *"time is right"* with respect to considering pharmaceutical agents..." [emphasis added] as new "non-lethal" weapons.<sup>169</sup>

The preface to the Applied Research Laboratory (ARL) report states that the literature study of incapacitating chemicals was carried out as "...an internally funded initiative and basis for discussion."<sup>170</sup> Both the Joint Non-Lethal Weapons Directorate (JNLWD) and the National Institute of Justice (NIJ) deny funding the report.<sup>171</sup> This is something of a moot point given the well-known close connections between the Applied Research Laboratory (ARL) at Pennsylvania State University, the JNLWD, and the NIJ. Nevertheless, it is clear from the timing of the publication that the research was closely tied to ongoing military developments.

The ARL report was published on 3 October 2000 and it was during a JNLWD review meeting held from 3 to 4 October 2000 that three new proposals were selected for funding under the JNLWD's Technology Investment Program (TIP) for fiscal year 2001, one of which concerned the further research on incapacitating agents by the US Army's Edgewood Chemical Biological Center (ECBC). The research effort, which would appear to build on the Pennsylvania State literature review, was announced in a 2001 JNLWD newsletter as follows:

Front End Analysis of Potential Non-Lethal Anti-Personnel Weapons [Soldier & Biological Chemical Command(SBCCOM)]: The objective is to identify feasible non-lethal chemical materials for further testing which have minimal side effects for immobilizing adversaries in military and law enforcement scenarios.<sup>172</sup>

This research project comprised:

...a series of workshops and analyses culminating in a database of potential riot control agents and calmatives, *with emphasis on technology advances in the past 10 years*.<sup>173</sup> [emphasis added]

It was scheduled for completion in the 3<sup>rd</sup> quarter of fiscal year 2002.<sup>174</sup> A little more information emerged on this research project in early 2003 when an item entitled 'Front End Analysis for Non-Lethal Chemicals. Fiscal Year 2001-2002 Technology Investment Project' appeared briefly on the JNLWD web site. It defined the project objectives as follows:

- Identify advances in the pharmaceutical industry and elsewhere for potential non-lethal applications
- Conduct military user workshops to identify range of desired operational effects
- Create a searchable database of potential candidates
- Provide a list of promising candidates to Judge Advocate General's office for preliminary legal review<sup>175</sup> [emphasis added]

Information on the findings of this research and on subsequent work is not available. A report of the US National Research Council's (NRC) study of "non-lethal" weapons science and technology, which was conducted during 2001 and 2002, was published in early 2003. It confirmed that US military research on incapacitating biochemical weapons was ongoing. Aware of the Army's 'Front End Analysis' study initiated in June 2000 at OptiMetrics, Inc. with funding from the Edgewood Chemical Biological Center (ECBC), the Applied Research Laboratory's literature review published in October 2000, and Joint Non-Lethal Weapons Directorate's 'Front End Analysis' study begun at ECBC in fiscal year 2001, the report noted that incapacitating agents were "under study by ECBC after lull in R&D for 10 years."<sup>176</sup> Researchers at ECBC had apparently returned to the sponge projectile soaked with a fentanyl derivative and antidote that Lawrence Livermore National Laboratory (LLNL) had proposed in the late 1990's. The 2003 National Research Council (NRC) report highlighted incapacitating chemicals as one of the major weapons technologies for further development. It noted that the main research and development issues would be "characterizing and quantifying the safety of the chemicals" and "obtaining the method of delivery that will provide the proper dose."<sup>177</sup> Despite concerns over compliance with the Chemical Weapons Convention (CWC) discussed in the report, major recommendations given by the National Research Council panel were to "increase research in the field of human response to calmatives", arguing: "Calmatives have potential as NLWs [non-lethal weapons] in many types of missions where calming of individuals or crowds is needed", and to "target efforts to develop chemical delivery systems".<sup>178</sup>

With the US military embarking on new research into incapacitating chemical weapons, the National Institute of Justice (NIJ) also funded further research in this area. Given the prior interconnections between military and law enforcement programmes on development of these weapons it is likely that there is close cooperation between the two groups. Furthermore a report of joint UK-US seminar on "non-lethal" weapons in 2000 makes clear that the US Department of Defense is even willing to sub-contract the development of weapons to other government agencies in order to circumvent international legal regimes such as the Chemical Weapons Convention. A recommendation in the report stated:

If there are promising technologies that DOD [Department of Defense] is prohibited from pursuing, set up MOA [Memorandum of Understanding] with DOJ [Department of Justice] or DOE [Department of Energy].<sup>179</sup>

In fiscal year 2001 NIJ funded a three phase project on "non-lethal" weapons at the Institute for Non-Lethal Defense Technologies (INLDT) at Pennsylvania State University (PSU). Phase two of the project was to "...conduct an investigation of controlled exposure to calmative-based oleoresin capsicum."<sup>180</sup> There is very little information available about this project, which involves the combination of incapacitating chemicals with OC irritant agent in order to produce more profound effects. However, a presentation by Joe Cecconi, the Senior Program Manager for the NIJ Less-Than-Lethal Technology Program, in February 2003 indicated that the project had been reviewed by a liability panel and that work was progressing at Pennsylvania State University.<sup>181</sup> A potential application of incapacitating agents for law enforcement was suggested by the Director of the National Institute of Justice (NIJ) in 2002. In response to concerns over commercial airline security following the events of 11 September 2001, the US National Institute of Justice (NIJ) completed a

report entitled *Less-Than-Lethal Weaponry for Aircraft Security*.<sup>182</sup> In a statement to the US House of Representatives on aviation security summarizing the conclusions she stated that:

Anesthetics or calmative chemicals could, in principle, be developed into a system whereby they could be remotely released into the cabin in order to incapacitate all passengers, and the hijackers, until the plane can be landed safely. Chemical systems of this type have not been employed in the field, however, and remain under study or in development.<sup>183</sup>

The same suggestion was made by the Director of the JNLWD in a presentation to the Airline Pilots Association in October 2001 in which he had argued that suitable incapacitating chemicals could be available in "3 years +".<sup>184</sup>

Since the 2003 National Research Council (NRC) report confirming renewed US military research on incapacitating agents there has been no further openly available information on the programme, due to likely classification of the ongoing work.<sup>185</sup> However, some documentation has emerged relating to the continued development of chemical delivery systems (see section 1.4.2 below). It is unclear whether these types of chemical weapons can now be accessed for US military operations. Two unconfirmed reports in 2003 quoted Rear Admiral Stephen Baker, the Navy's former Chief of Operational Testing and Evaluation, as saying that US Special Forces had "knock-out" gases available for use in Iraq.<sup>186</sup>

The 2006 announcement for research and development proposals in support of the Joint Non-Lethal Weapons Program (JNLWP) made no mention of incapacitating agents or any other chemical agents. Although a major goal put forward was the development of "next generation", "non-lethal" weapons and payloads for "*extended duration incapacitation* of humans and material at ranges in access [sic] of small arms range".<sup>187</sup> [emphasis added]

For details of the most recent military interest in incapacitating agents it is necessary to look at events and activities in other countries.

#### Russia

In late 2002, just as the National Research Council (NRC) of the National Academies was preparing to publish its' report on "non-lethal" weapons recommending the further research and development of incapacitating biochemical weapons, it emerged that at least one country had already developed and deployed such weapons and was willing to use them within its' own borders and on its' own citizens. On 23 October 2002 a group of around 50 armed men and women claiming allegiance to the Chechen separatist movement took control of the Dubrovka theatre in Moscow, taking over 800 people hostage during a performance of the musical 'Nord Ost' and demanding the withdrawal of Russian troops from Chechnya. In the morning of the third day of the siege, 26 October, Russian authorities pumped an aerosolised chemical incapacitating agent into the auditorium through the ventilation system. Allowing at least 30 minutes for the agent to take affect on hostages and hostage-takers alike, Special Forces stormed the building shooting the majority of the hostage takers, some of whom were wrapped in explosives, whilst unconscious.<sup>188</sup> At least 129 hostages were killed and many survivors needed hospital treatment; (*The Guardian* reported in October 2003 that the death toll might be even higher).<sup>189</sup> All but one or two died due

to exposure to chemical agent.<sup>190</sup> It was not until four days later that that the Russian Health minister finally released the identity of the agent used, stating that it was "based on derivatives of fentanyl" and refusing to provide any further information.<sup>191</sup> The main side effect of fentanyl derivatives is respiratory depression, which is thought to have been the major factor in the death of so many in Moscow. Although there is some debate as to whether the agent used was a mixture of a fentanyl derivate and another inhalation anaesthetic such as halothane or perhaps even a novel agent, it seems certain that the aerosol contained an opioid agent since victims were treated with naloxone.<sup>192</sup> Indeed a 2003 paper authored by three US medical toxicologists and discussing the implications of events in Moscow commented:

In the United States, naloxone, for a long time a critical antidote to treat heroin overdose and iatrogenic opioid toxicity, has now become a crucial component of our chemical warfare antidote repository.<sup>193</sup>

Various reports have suggested that the agent used was either sufentanil, remifentanil, or the most potent fentanyl analogue, carfentanil.<sup>194</sup> Experts in these anaesthetic compounds who have been involved in the US Army's programme to develop incapacitating agents, namely former Army researcher C. Parker Ferguson and Prof. Theodore Stanley from the University of Utah, and also Prof. James Woods at the University of Michigan, have argued that the most likely compound used was carfentanil.<sup>195</sup> Due to the size of the theatre in Moscow the agent would need to have been extremely potent with a low concentration needed for the effect (otherwise filling the space with agent would have taken too long). According to Ferguson only three classes of drug are sufficiently potent: fentanyl derivatives such as carfentanil and sufentanil, the oripavines such as the wildlife tranquilizer etorphine (trade name: M99/Immobilon), and benzimidazoles such as etonitazene. All of these are opioid drugs, which have been considered in past US and UK military incapacitating agent research and development programmes. He argues that the first choice would be fentanyl derivatives, not only because of their potency but also because of their "demonstrated effectiveness as an aerosol".<sup>196</sup> In a paper published by Prof. Stanley in 2003 following the Moscow siege he argued that carfentanil was the most likely candidate since it is the most potent derivative:<sup>197</sup>

Carfentanil's potency makes it feasible as a candidate to immobilize hundreds of people in a large auditorium. An extremely potent material such as carfentanil would best explain the rapid, effective immobilization of the occupants of the auditorium.<sup>198</sup>

However, other observers have claimed that the agent used by the Russians was called M99, an alternative name given to etorphine (trade name Immobilon), which, like carfentanil (trade name Wildnil), has long been used to immobilize large animals. It is also antagonised (or reversed) by naloxone. A paper at the  $2^{nd}$  European Symposium on Non-Lethal Weapons in May 2003 by John Alexander, claimed that the agent used was called M99.<sup>199</sup>

As events in Moscow illustrated, Russia clearly has a significant programme to develop incapacitating biochemical weapons and, moreover, a deployable capability. A paper by Russian scientists given to the  $2^{nd}$  European Symposium on Non-Lethal Weapons in May 2003 addressed future perspectives for the use of "non-lethal" weapons in Europe, noting that experience in the use of these agents had been gained in Moscow but that further research was needed:

There has been significant success in the chemistry of calmatives, although the restriction of individual dosage is very important. There is still no perfect tranquillizing agent, but the problem of safety can be solved by the succeeding or simultaneous application of calmative and antidote. This can minimize potential fatality.<sup>200</sup>

Of course this strategy of mixing agent and antidote (agonist and antagonist) has been a common characteristic of US incapacitating agent development efforts.

Ongoing Russian research in this area was also presented to the 3<sup>rd</sup> European Symposium on Non-Lethal Weapons in May 2005. A paper entitled *Principles of Modelling of the Scenario of Calmative Application in a Building with Deterred Hostages* describes computer modelling and simulation of pumping aerosolised chemical agents into buildings to incapacitate hostages and hostage takers alike. The authors acknowledge that in reality the incapacitation of those inside the building cannot be carried out effectively without killing people because the agent does not disperse evenly within the building and those inside receive a cumulative dose over time:

If the level of 95% efficiency is absolutely required to neutralize terrorists and to prevent mass destruction, there is no chance to eliminate hard consequences and fatalities. Calculations show that the majority of hostages can get serious poisoning and part of them – fatality. This is the cost of releasing if no other solutions left.<sup>201</sup>

Following the use of the incapacitating agent in Moscow in 2002 there was speculation about the status of Russian development of these weapons. It appears that their deployment was not a 'one off' and that such weapons may be stockpiled for rapid deployment when required. A Russian news source reported that the opioid antidote naloxone was made available to doctors during the 2004 school siege in Beslan in anticipation of Special Forces using narcotic agents again.<sup>202</sup> On 13 October 2005 militants carried out attacks in the Russian town of Nalchik. Russian Special Forces were deployed to the town, and during the second day of fighting Russian NTV reported that they used a "knockout gas" against militants who were holding hostages in a shop.<sup>203</sup> There was no information about the nature of the chemical used. However, it was reported that victims of the attack were administered an antidote.<sup>204</sup>

## Czech Republic

The only openly available information about current research and development of biochemical incapacitating agents is that published by Czech researchers. In 2005 it emerged that the Czech military were funding the development of these weapons. At the 3<sup>rd</sup> European Symposium on Non-Lethal Weapons in Ettlingen, Germany in May 2005 a paper was presented entitled *Pharmacological non-lethal weapons*.<sup>205</sup> The authors were Professor Ladislav Hess, from the Institute for Clinical and Experimental Medicine in Prague, Dr. Jitka Schreiberova, formerly of the Department of Anaesthesia at the University Hospital in Hradec Kralove and now Chief anaesthesiologist in the Department of Neurosurgery at Charles University Prague, and Dr. Josef Fusek, from the Czech Army's Purkyne Military Medical Academy in Hradec Kralove. The work apparently began some years ago in 2000,<sup>206</sup> and previous research was published in a Czech Journal.<sup>207</sup> Schreiberova and Hess also presented their research as an abstract to the Annual Meeting of the European Society of

Anaesthesiology in Vienna in late May 2005<sup>208</sup> and in October 2005 to the Jane's 8th Annual Less-Lethal Weapons Conference in Leeds, UK.<sup>209</sup> The research, to develop sedative and anaesthetic agent combinations for use as weapons, has been funded by the Czech Army under Project No: MO 03021100007 assigned to Dr. Fusek.<sup>210</sup> In the introduction to their 2005 paper the authors argue: "There is a possibility of pharmacological control of an individual behaving aggressively".<sup>211</sup>

The types of drugs considered by Hess *et al.* are similar to those highlighted in the Pennsylvania State University report from 2000,<sup>212</sup> as described in the introduction to the paper:

They are highly receptor-specific agents with a well controllable effect. They are commonly used in anesthesiology practice and include benzodiazepines (midazolam), opioids (fentanyl and its derivatives), and alpha2 agonists (dexmedetomidine). There are specific antagonists to all these agents like flumazenil, naloxone or naltrexone and atipamezole. An important group of agents for these purposes are dissociative anesthetics (ketamine).<sup>213</sup>

The Czech paper describes the results of experiments with rhesus monkeys over several years in which they injected the animals with different mixtures of drugs to determine combinations and doses that would result in what they termed "fully reversible immobilization". In these experiments they administered the agents through intramuscular injection measuring the time to onset of effect, the time to immobilization, and the rate of recovery. Various combinations of medetomidine, ketamine, midazolam, dexmedetomidine, fentanyl, and hyaluronidase (an enzyme that speeds up absorption) were tested. The synergistic interactions of some of these drugs were incorporated into the experiments, such as the use of midazolam to decrease the effective dose of other drugs. One mixture, comprising midazolam, dexmedetomidine and ketamine, was tested on ten nurses who were paid to participate in the experiments.<sup>214</sup> Following intramuscular injection the time taken for the subject to have to lie down was considered as the "immobilization time", which in their experiments varied from two to four minutes. Another mixture of dexmedetomidine, midazolam, and fentanyl was tested on patients prior to surgery. Further experiments in rabbits employed opioids, including remifertanil, alfentanil combined with low doses of naloxone and etorphine combined with the antagonist butorphanole.

The paper also describes tests with animals on various routes for delivering these agents, including nasal, transbuccal (across oral mucous membranes), and conjunctival (across the eye). The aerosol route of delivery was tested with rats and subsequently with "volunteers", who were in fact children in hospital. They used a spray in tests with two different combinations of agents: ketamine and dexmedetomidine, and ketamine and midazolam. Transdermal delivery (across the skin) was tested in rabbits with etorphine (Immobilon) combined with the solvent dimethyl sulphoxide (DMSO), which facilitates absorption through the skin. They also tested a mixture of ketamine, detomidine and midazolam combined with DMSO and planned to experiment with a mixture of the dissociative anaesthetic tiletamine and zolazepam (trade name Telazol) together with DMSO. The authors propose that incapacitating agents could be delivered in this way operationally:

The transdermal technique of administration could possibly be used to induce long-term sedation with  $alpha_2$  agonists, benzodiazepines, and a combination of them to pacify aggressive individuals. Using the paint-ball gun principle, anesthetic-containing balls could

be used. Impact of the ball would be followed by their destruction and absorption of garment with the anesthetics which will be quickly absorbed via the skin.<sup>215</sup>

As discussed earlier in this paper, in the mid 1990's Lawrence Livermore National Laboratory (LLNL) in the US were proposing the very same technique having discounted the idea of a dart gun.<sup>216</sup> By 1997 LLNL were looking at a similar transdermal delivery system incorporating a fentanyl-soaked sponge projectile, <sup>217</sup> which was again under investigation by the US Army in 2001 when the National Research Council (NRC) were conducting their study of "non-lethal" weapons.

Clearly the Czech research has taken inspiration from prior studies conducted as part of the US programme. Furthermore, an idea of the broader international interest in their research can be garnered from NATO's support for this chemical weapons development effort. The panel on the human effects of "non-lethal" weapons (HFM-073) at NATO's Research and Technology Organisation (RTO) reviewed the Moscow incident favourably,<sup>218</sup> and the Chair of that panel has expressed support for the Czech research.<sup>219</sup> The Czech representative to the NATO HFM-073 panel was, for some time, Dr. Joseph Fusek, co-author of the paper on *Pharmacological Non-Lethal Weapons*.<sup>220</sup> Dr. Fusek works at the Czech Army's Military Medical Academy where he specialises in defensive measures against chemical agents. In 2004 he co-authored a paper entitled *Chemical Agents and Chemical Terrorism*, which warned of potential terrorist use of various chemical weapons including incapacitating agents, although did not mention his role in the development of these weapons.<sup>221</sup> There appears to be considerable interest in incapacitating agents within the Czech military. Two papers were published in 2004 on this subject by Fusek and colleagues.<sup>222</sup>

At the time of writing Hess, Screiberova, and Fusek were set to present another paper concerning their ongoing research on incapacitating agents to the 4<sup>th</sup> European Symposium on Non-Lethal Weapons, entitled *Drug-Induced Loss of Aggressiveness in the Macaque Rhesus*.<sup>223</sup>

## **Other Countries**

It is likely that research and development on incapacitating agents is ongoing in other countries aside from the US, Russia, and the Czech Republic. However, there is no information available describing specific programmes. This may be due to the secretive nature of this type of research. In 2004 The Sunshine Project published a report entitled Biological and Biochemical Weapons Related Research in France, which included an assessment of French interest in this area.<sup>224</sup> The report points to military research investigating the behavioural and cognitive effects of various psychoactive and anaesthetic compounds, however it notes that researchers did not find any indication of an incapacitating agent programme. Nevertheless a 2003 opinion piece in the French publication Le Monde Diplomatique by Prof. Chantal Bismuth, a leading toxicologist, and Col. Patrick Barriot, a military medic specialising in anaesthesiology, describe the likely militarization of drugs, saying that 'the chemical weapons of tomorrow may be found within medical dictionaries of drugs.<sup>225</sup> They were co-authors of a subsequent paper in 2004 entitled, *Chemical* Weapons: documented use and compounds on the horizon, which gives further indication of French interest. One section of the paper describes the 2002 Moscow theatre siege, warning that the dangers of using incapacitating chemical weapons in such a hostage situation "must not be underestimated", but it is apparently supportive of their continued development:

... there is certainly a future for "calmative" drugs in this scenario. Publication of these data demands caution as the terrorists themselves could use these new indications and methods. Other means of personnel control are under study, including use of microwaves and acoustic weapons. *Secrecy in this research is essential for their future efficacy*.<sup>226</sup> [emphasis added]

The UK appears to be less interested in incapacitant development if we are to judge by the 2004 report of the Northern Ireland Office (NIO) Steering Group investigating alternatives to the baton round for policing. Work on incapacitating chemical agents, called "calmatives" in the report by the Police Scientific Development Branch (PSDB) – now Home Office Scientific Development Branch (HOSDB) - has been downgraded from Category B to Category C. The latter category is defined as including "…technologies that were not considered of immediate interest or importance."<sup>227</sup> The report states "… that use of calmatives in policing situations would not be a straightforward process"<sup>228</sup> and explains that the use of any drug would require knowledge of the subject's medical history. Nevertheless the Home Office is not ruling out this type of weapon for the future and the following caveat is given in the report:

PSDB will continue to monitor this area, focussing on international research programmes and future developments in delivery methods and potential tranquilising agents.<sup>229</sup>

As regards the UK military, the Ministry of Defence and the US Department of Defense have collaborated on "non-lethal" weapons, including related wargaming,<sup>230</sup> through a Memorandum of Understanding signed in February 1998.<sup>231</sup> The report of the US/UK Non-Lethal Weapons (NLW)/Urban Operations Executive Seminar in November 2000 illustrates the differing positions of the UK and the US as regards the prohibitions of the Chemical Weapons Convention (CWC). The UK position does not support the military development of incapacitating biochemical weapons.<sup>232</sup>

#### **1.4.2 Delivery Systems**

The US military has long desired to increase the range of various "non-lethal" weapons by developing new delivery systems.<sup>233</sup> Many of these delivery systems are being designed to deliver chemical agents although the discussion of payloads is often non-specific and a variety of possibilities have been mentioned including irritant chemical agents (riot control agents), malodorants, anti-traction chemicals, and incapacitating agents. This ambiguity allows delivery system development to progress whilst minimising criticism of renewed military interest in biochemical weapons. Nevertheless they are clearly being considered for the delivery of incapacitating agents, as the 2003 National Research Council (NRC) report noted:

Although a number of promising chemical non-lethal weapons technologies exist, most of them lack a suitable delivery system. Few reliable, low-risk, and low-cost methods exist for delivering and dispensing chemical NLWs precisely and accurately. ... It becomes critical in the delivery of calmatives, where proper doses must be achieved.<sup>234</sup>

Even if these delivery systems are justified on the basis of use of riot control agents for "law enforcement including domestic riot control", serious concerns have been expressed that many of the munitions under development are not suitable for this purpose, including mortar rounds with a range of 2.5 km and an artillery projectile with a range of 28 km.  $^{235}$ 

In addition to the systems described in the following sections there are numerous delivery systems and associated technologies available for irritant chemical agents such as CS and OC that have a long history of development including projectiles, grenades, smoke generators,<sup>236</sup> and spray devices. Many of these may be adaptable or applicable to the delivery of incapacitating agents. In some situations an aerosol generator may be used rather than a munition or spray device, as illustrated by the 2002 theatre siege in Moscow.

#### **Projectiles**

Paintball-type encapsulated projectiles were considered for delivery of incapacitating agents by Lawrence Livermore National Laboratory (LLNL) researchers and recently the idea has been proposed by Czech researchers. Such frangible projectiles and associated compressed air launchers are already in widespread use by police forces in the US for the delivery of powdered irritant agents such as CS, OC, or PAVA against individuals. There are two main weapons systems available. One the PepperBall system, which has been in use since 1999, and the other is the FN303 system made by FN Herstal.<sup>237</sup> The FN303 is in use by the US Army and currently it has been designated the Individual Serviceman Non-Lethal System (ISNLS).<sup>238</sup> These are the types of projectiles that may be adapted for delivery of incapacitating agents against individuals.

During the late 1990's the US Department of Justice began a project to reinvent the ring airfoil projectile (RAP), a rubber projectile developed by the US Army in the 1970's which would release a three foot cloud of irritant agent upon impact from compartments inside the projectile. This project to develop the projectile and a multi-shot launcher with a range of 50 metres is ongoing. In addition to the consideration of the irritant agent OC, it has also been proposed for the delivery of incapacitating agents. A 2002 proposal to continue development of this system, which was accepted by the National Institute of Justice (NIJ), stated:

Included in this proposal is the intention to successfully demonstrate a payload-delivering Ring Airfoil Projectile. First effort would concentrate on delivery of a chemical payload on and about the target. Payloads of *incapacitants*, irritants, malodorants, and marking agents would be of first interest, and could lead to a family of Ring Airfoil LTL [Less-Than-Lethal] rounds.<sup>239</sup> [emphasis added]

Further development of this projectile, now termed Advanced Segmented Ring Airfoil Projectile (ASRAP), was funded in 2004.<sup>240</sup> Furthermore this projectile was undergoing testing by the Advanced Research Laboratory at Pennsylvania State University as of 2004.<sup>241</sup> It is possible that the RAP or ASRAP is being considered for delivery of mixtures of the irritant OC and incapacitating agents, as studied at Pennsylvania State on behalf of the National Institute of Justice (NIJ).

#### "Non-Lethal" Munitions

Relevant research and development conducted by the US military relates to delivery of chemical agents at long range and over wide areas to target groups of people (as opposed to projectiles targeted at individuals). A proposal to develop an Overhead Chemical Agent Dispersion System (OCADS) was accepted for funding during fiscal year 1999 under the Joint Non-Lethal Weapons Directorate's (JNLWD) Technology Investment Program (TIP). The name of the project was later changed to Overhead Liquid Dispersion System (OLDS). The purpose of the development effort was to provide the US military with: "...the ability to rapidly disperse chemical agents over large areas. The dispersed agents can be used for crowd control or to provide a remotely generated protective barrier."<sup>242</sup> This work was carried out by Primex Aerospace Company (since acquired by General Dynamics) in collaboration with the US Army's Armament Research, Development and Engineering Center (ARDEC) at Picatinny Arsenal, New Jersey. The final report, published in April 2000, described the successful design, testing, and demonstration of a system comprising a launcher and dispersal device. The dispersal device itself consists of a liquid canister made of plastic with integrated gas generator to disperse the payload.<sup>243</sup> The demonstrated device could spray the liquid over a circular area of 12m in diameter at ranges over 100m. According to the report the device was under development with a view to dispersing OC but the technology is adaptable for delivering liquids with differing properties in varying droplet sizes (from 1cm to vapour) and for delivering powders, encapsulated liquids, or projectiles such as rubber pellets. It is also scalable for different distances and smaller or larger areas of dispersion.<sup>244</sup> Subsequently, in September 2001, the Solid Propellant Systems Group at General Dynamics Ordnance and Tactical Systems (formerly Primex Aerospace Company) was funded by JNLWD to carry out further work building on the Overhead Liquid Dispersion System (OLDS) to develop similar liquid dispersal technology for an 81mm "non-lethal" mortar in collaboration with ARDEC.<sup>245</sup> By late 2003 this work was ongoing and Edgewood Chemical Biological Center (ECBC) had begun a study of potential malodorant payloads.<sup>246</sup>

JNLWD began funding this ongoing project, managed by ARDEC, to develop a 81mm "non-lethal" mortar under the fiscal year 1999 Technology Investment Program (TIP), with work carried by United Defense, the Army Research Laboratory (ARL), and the Army's Edgewood Chemical Biological Center (ECBC).<sup>247</sup> The Applied Research Laboratory at Pennsylvania State University has also been involved in the assessment of this weapon.<sup>248</sup> The development aim is a mortar that can deliver a solid, liquid, aerosol or powder payload from 200 m up to 2.5 km from the target with a casing that does not cause any injury through kinetic impact on the target person(s).<sup>249</sup> One prototype incorporated a parachute system that activates above the target just before the payload is released to slow the descent of the munition casing and it has already been through a 'proof-of-principle' test at a range of 1.5 km.<sup>250</sup> Another approach researchers are pursuing is a munition with a frangible casing. Tests were conducted in November 2002 and February 2003 on both frangible and non-frangible versions of the mortar including tests of liquid dispersal and with CS irritant simulants, the aim being to cover an area of 25 m<sup>2</sup>.

Another type of munition, under development by the Army's Armament Research, Development and Engineering Center (ARDEC) for JNLWD, and designed to carry chemical payloads is the Airburst Non-Lethal Munition (ANLM), which is being developed under a wider programme to produce a new assault rifle for the US Army called the Objective Individual Combat Weapon (OICW). The current prototype OICW is called the XM29 integrated airburst weapon. The XM29 is primarily a lethal weapons system, firing both conventional bullets as well as airburst munitions with high explosive, thermobaric (fuel-air explosive), or flechette (multiple nail-like metal projectiles) payloads.<sup>251</sup> A related XM25 system will fire the airburst munitions only.<sup>252</sup> The Airburst Non-Lethal Munition forms part of this programme and is designed to burst open just before it reaches its' target, releasing the payload contained inside.<sup>253</sup> The aim is to develop a munition that could be used at ranges of 5 to 1000 m.<sup>254</sup> According to an Army presentation in 2001 there were a variety of potential anti-personnel payloads including incapacitating agents.<sup>255</sup> Another indication of the potential employment of incapacitating chemical agents was given in the 2003 National Research Council Report on "non-lethal" weapons which observed:

Current activities ... include the development of a 20-mm NLW round for the objective individual combat weapon (OICW). This round is designed to provide an airburst, dispensing liquid aerosols or powders of *calmatives*, lacrimators, or malodorants; antitraction chemicals; and/or markers to counter personnel or clear facilities.<sup>256</sup> [emphasis added]

Initial testing by the US Army's Armament Research, Development and Engineering Center (ARDEC) and Edgewood Chemical Biological Center (ECBC) was conducted in January and April 2002 with various CS irritant chemical payloads.<sup>257</sup> Shortly afterwards the Applied Research Laboratory at Pennsylvania State University was tasked with conducting a technology assessment of the Airburst Non-Lethal Munition (ANLM). Their assessment states that the underlying technologies for the munition exist but that one of the major areas for attention is the payload. Referring to the CS payload they express doubts over its' effectiveness in the small quantities delivered by a 20mm munition and assert that "There may be better and more concentrated agents. Moreover, new agents are continually emerging."<sup>258</sup> Furthermore they recommend that a 'Front End Analysis' of potential agents be conducted, arguing:

This helps identify potential payloads that might meet user needs and intended effectiveness. It also evaluates the relative merits of each payload. This analysis could be especially helpful in meeting intended incapacitation effects, which have often been sought for non-lethal weapons. ... Specifically, it might identify *very concentrated agents*, well suited for a [REDACTED] mm munition payload.<sup>259</sup>

It seems reasonable to assume that these references to "new" and "concentrated agents" and desired "incapacitation effects" relate to incapacitating agents rather than riot control agents (RCAs), especially given the fact that two of the authors of the ANLM assessment also authored the 2000 Pennsylvania State University report, *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*.<sup>260</sup>

Work on the design of the ANLM munition has continued<sup>261</sup> and an October 2006 JNLWD 'fact sheet', which makes no reference to development of chemical agent payloads, notes that there are three versions under development:

A low-velocity 40mm variant is being designed for man-portable grenade launchers. Two high-velocity variants (25mm and 40mm) are also being designed for crew-served and mounted systems. The high-velocity variants will possess the capability to achieve ranges greater than that of small arms.<sup>262</sup>

The US Army's ARDEC is also taking the lead in development of another munition in collaboration with General Dynamics Ordnance and Tactical Systems who are also developing the Overhead Liquid Dispersal System (OLDS) described above. This is a large 155mm artillery projectile or 'cargo round' called the XM1063, which is adapted to carry a liquid payload.<sup>263</sup> To give some idea of the size and range, this munition is based on the 155mm M864, which carries 72 conventional grenades at ranges of up to 28km.<sup>264</sup> The XM1063, also referred to as the Non Lethal Personnel Suppression Projectile, will carry multiple submunitions at this range, which will be released above the target area and then fall to the ground via parachute and disperse their liquid payloads,<sup>265</sup> covering a minimum area of 5,000 square metres.<sup>266</sup> General Dynamics is focussing on development of the submunitions, likely incorporating their overhead liquid dispersal technology.<sup>267</sup> Details of the proposed payload are scant but the available documentation describes it as a "personnel suppression payload".<sup>268</sup> There is no indication as to the exact nature of the liquid, although a September 2004 contract announcement noted:

Payload agent effectiveness includes engineering support and test hardware support for payload agent concentration, area coverage, and payload agent effectiveness testing at the Army Edgewood Chemical Biological Center.<sup>269</sup>

Therefore the anti-personnel liquid payload will certainly be some kind of chemical agent.<sup>270</sup> When General Dynamics Ordnance and Tactical Systems won the contract to support initial testing of this munition by ARDEC in 2004 potential payloads had apparently already been developed for use in testing.<sup>271</sup> After test firings in fiscal years 2005 and 2006, a follow on contract was awarded to General Dynamics in August 2006 for continued development in support of further demonstration tests in fiscal year 2007.<sup>272</sup>

In addition to these delivery systems under development, Edgewood Chemical Biological Center (ECBC) have patented several other devices for dispersing chemical agents. A February 2003 patent for a Rifle-launched non-lethal cargo dispenser<sup>273</sup> to deliver aerosols (Patent No. 6,523,478) included amongst possible payloads both chemical and biological agents. Following pressure from The Sunshine Project, who noted that such a device would contravene the Biological Weapons Convention (BWC),<sup>274</sup> a divisional patent<sup>275</sup> was accepted (Patent No. 6,668,032 of February 2004).<sup>276</sup> It is identical to the original patent apart from small changes also relating to potential payloads and their legality.

The projectile of claim 4, wherein the aerosol composition is further selected from the group consisting of smoke, crowd control agents, biological agents, chemical agents, obscurants, marking agents, dyes and inks, chaffs and flakes. [Patent 6,523,418]

The projectile of claim 1, wherein the aerosol composition is further selected from the group consisting of smoke, crowd control materials, obscurants, marking materials, dyes and inks, chaffs and flakes. [Patent 6,688,032]

Other references to "crowd control agents, biological agents, chemical agents" elsewhere in the Patent language have also been replaced with the rather unspecific phrase "crowd control materials".<sup>277</sup>

An additional relevant patent is No. 6,802,172 for a 'Particle aerosol belt', an aerosol delivery system apparently designed to deliver payloads including "pharmaceutical

compositions".<sup>278</sup> The patent contends that "Aerosols are used in the military to defensively position and protect combat forces" and "In civilian use, aerosols are dispersed by police as a non-lethal means for crowd control dispersal, riot control, personal protectants and/or *incapacitating agents*."<sup>279</sup> [emphasis added].

Another weapon relevant to the delivery of chemical agents is a modular grenade designed by Scientific Applications and Research Associates Inc. (SARA), which was originally developed under the Joint Non-Lethal Weapons Directorate's (JNLWD) 'Clear-A-Space Program'. It has been called the Multi-Sensory Grenade and more recently the Multi-Functional Grenade. Various propositions of payloads have been suggested including bright light, loud noise, and chemicals such as irritant agents and malodorants.<sup>280</sup> The US National Institute of Justice (NIJ) has also shown interest in this device, funding an evaluation of its' potential use to control the movement of individuals or crowds.<sup>281</sup> The Sunshine Project obtained a heavily redacted 2004 contract detailing a project funded by NIJ for SARA to develop a computer simulation of "non-lethal" weapons usage scenarios including those incorporating the Multi-Function Grenade. One example describing the simulation suggests interest in incapacitating agents:

Here, we see a gas-masked soldier in position near a building's air supply intake. With appropriate additions to the program, we can have the soldier's weapon-usage abilities allow for the application of *knockout-gas* or other less-than-lethal methods. [emphasis added]<sup>282</sup>

#### **Unmanned Aerial Vehicles**

Unmanned aerial vehicles (UAVs) are under development primarily for military tasks such as lethal weapons delivery, sensing, and reconnaissance and it is a field of significant investment. The US Department of Defense invested over \$3 billion in this area during the 1990's and planned to increase this to over \$16 billion during the 2000's.<sup>283</sup> A very small but significant area of interest is the use of UAVs to deliver various "non-lethal" payloads at long distances,<sup>284</sup> including chemical agents. In the mid-1990's a "non-lethal" dispenser system was developed by the US Naval Surface Warfare Center Dahlgren Division (NSWC-DD) in collaboration with the Marine Corps Warfighting Laboratory (MCWL). Tests were carried out by the Joint Non-Lethal Weapons Directorate (JNLWD) with both Hunter and Exdrone UAVs during 1996 and 1997 using smoke muntions to simulate irritant chemical agent munitions.<sup>285</sup> A paper entitled Unmanned Aerial Vehicle (UAV) Non-Lethal (NL) Payload Delivery System, presented at the Non-Lethal Defense III conference in 1998, described these tests, reporting that a UAV-dispenser system could be used with any UAV with a 40 lb or more payload capability.<sup>286</sup> This project was prioritised by the JNLWD during their 1998 review of existing programmes.

The Joint Non-Lethal Weapons Directorate also funded the development of an unmanned platform to spray liquid payloads by remote control at the Southwest Research Institute (SwRI):

SwRI engineers developed a computer-controlled unmanned powered Para foil (UPP) equipped with a payload that dispenses liquid spray while in flight. Developed for the Marine Corps Non-Lethal Directorate, the system is intended to provide non-lethal crowd control options for the U.S. military. The UPP was fitted with a pan-tilt camera to continually locate the impact point of the liquid spray. Using computer-assisted flight modes and the camera image, a remote operator can direct the UPP over a target at low altitude and release the spray.<sup>287</sup>

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Furthermore under the JNLWD's Technology Investment Program for fiscal year 1999 Raytheon were tasked with assessing the feasibility of using their Extended Range Guided Munition (ERGM)<sup>288</sup> to deliver "non-lethal" payloads including chemical agents. Another Technology Investment Program project was the study of a so called Loitering Submunition for autonomous delivery of "non-lethal" payloads.<sup>289</sup> A major recommendation of the National Research Council (NRC) panel was for further development of unmanned vehicles to deliver "non-lethal" weapons including chemical agents at long distance with greater accuracy.<sup>290</sup>

#### *Microencapsulation*

In 1999 the Joint Non-Lethal Weapons Directorate (JNLWD) funded a project at the Advanced Polymer Laboratory (APL) at the University of New Hampshire to carry out research in to the use of microencapsulation for delivery of chemical agents. Proposed chemicals included incapacitating agents such as anaesthetic drugs.<sup>291</sup> Reasons for encapsulating chemicals include enabling controlled release and compartmentalization of binary systems. In addition they could be delivered from a variety of platforms such as shotguns, launchers, airburst munitions, mortars, and UAVs. Microcapsules may vary in size from centimetres to microns in diameter depending on the applications. Small microcapsules could even be inhaled for delivery of incapacitating agents. The researchers at the University of New Hampshire demonstrated a number of secondary release mechanisms that could be used to control the release of the materiel inside the capsule including mechanical rupture (weight of a human), thermal release (temperature activation), and hydrolytic release (water dissolves capsule).<sup>292</sup> According to the Advanced Polymer Laboratory (APL) web site, encapsulated irritant agents, malodorants, and dyes have already been developed.<sup>293</sup> In addition to work on microcapsules the APL has carried out other work for the JNLWD, designing a shell in support of the "non-lethal" mortar development programme discussed above.<sup>294</sup> Microencapsulation is clearly seen as a potential technological approach to targeting and controlling delivery of chemical agents, as the National Research Council (NRC) panel argued in 2003:

Special packaging techniques such as microencapsulation should be explored because they may be useful in creating new, more deliverable forms of chemical NLWs.<sup>295</sup>

#### **1.5 Assessment**

#### **1.5.1** Technical Barriers

This analysis illustrates that there have been a succession of failures to develop biochemical incapacitating weapons, beginning with US and UK efforts during the Cold War. Despite great investment in a programme which spanned over twenty five years in the US and that incorporated extensive human experimentation, a significant incapacitating agent capability did not emerge. In their assessment of the US and UK programmes Dando and Furmanski concluded: "...the effort in the West to find a non-lethal chemical incapacitant during the Cold War was a distinct failure."<sup>296</sup> LSD was discounted and Sernyl or phencyclidine (PCP) was approved for production but was never weaponised. Although BZ was produced and weaponised in the early 1960's, it was never fully integrated into the US chemical weapons arsenal due to the
deficiencies of both the agent and the delivery system. Although another agent had been identified to replace BZ by the mid-1970's it was never weaponised and the BZ weapons were declared obsolete. After a lull during which the US programme continued at a low level, military and law enforcement interest in incapacitating agents increased in the late 1980's. However, the Army's concerted effort to produce an Advanced Riot Control Agent Device (ARCAD) in the early 1990's also faltered, as did the related National Institute of Justice (NIJ) research effort. On the basis of available information, the revived contemporary US military programme has yet to succeed in producing such a weapon. Although some proponents welcomed the Russian use of a fentanyl derivative weapon in Moscow in 2002 and contended that it produced a better result than could have been expected with other types of force,<sup>297</sup> this event too exhibited the failure thus far to develop an incapacitating biochemical weapon that does not endanger life or risk serious injury in operational conditions.

During the 1960's UK military researchers acknowledged the deficiency in their knowledge of the interaction between biochemical agents and receptors in the central nervous system. This meant that the search for new agents had to be carried out by trial and error rather than by design, reflecting the process of drug discovery at the time. This in turn made it very difficult to elicit specific effects. For contemporary efforts to develop such a weapon these particular concerns have been ameliorated with an exponential increase in the understanding of receptor structure and function. The 1980's saw the identification of numerous peptide neurotransmitters that mediate chemical transmission in the nervous system alongside 'classical' neurotransmitters such as acetylcholine. However, it is advances during the past 10-15 years that have revolutionized the field. This progress was particularly marked during the 1990's, dubbed the 'Decade of the Brain', when there were more advances in neuroscience than all previous years combined.<sup>298</sup> The impact of genomics has led to a greater understanding of receptor systems and the elucidation of the structure and function of certain receptor sub-types that have now become potential targets for therapeutic drugs or indeed incapacitating agents. The key issue in relation to this change is specificity, something that was lacking from early incapacitating agents under consideration such as BZ, as Dando has illustrated using the example of acetylcholine receptors:

When efforts were being made to produce effective incapacitants like BZ during the Cold War period it was known that there were two different types of acetylcholine synapse [nicotinic and muscarinic]. ... The difficulty those engaged in developing weapons in the Cold War era had was that they did not know what we now know, that there are nine sub-types of nicotinic and five sub-types of muscarinic receptor. The muscarinic sub-types are the most important in the brain. Clearly, without such knowledge, designing a reliable incapacitant was almost impossible and BZ was eventually rejected as too variable in its effects.<sup>299</sup>

However, by 2000 the Pennsylvania State researchers observed:

It was noted that drugs can be tailored to be highly selective and specific for known receptor (protein) targets in the nervous system with unique profiles of biological effects on consciousness, motor activity and psychiatric impact.<sup>300</sup>

Tailoring drugs for specific receptor targets has become easier through the emergence of combinatorial chemistry to create large 'libraries' of potential compounds and high-throughput screening techniques to assess their activity. Moreover bioinformatics and computational biology permitting large-scale analysis of biological data have enabled development of computer modelling software that can be used to carry out virtual screening to identify new compounds.<sup>301</sup> As well as offering the opportunity to develop more effective new drugs to treat a variety of mental illnesses, as is a priority of the global pharmaceutical industry, this knowledge is of course dual use.<sup>302</sup> The US incapacitating agent development programme has closely shadowed advances in the pharmaceutical industry and recently developers have advocated close collaboration with industry for ongoing efforts akin to past industrial liaison programmes.

An enduring barrier to development of incapacitating agents, interrelated with the issue of specificity, has been the problem of finding compounds with an adequate safety margin; that is a sufficiently wide difference between the dose of an agent which effectively incapacitates and the dose that kills. In pharmacological terms the safety margin is defined as the therapeutic index, which represents the ratio of the mean lethal dose (LD50) to the mean effective dose (ED50). The higher the therapeutic index (LD50/ED50) the higher the safety margin. The central requirements of an incapacitating agent are that it be sufficiently potent to be logistically feasible, thereby inducing the desired effect with a small dose, as well as having a wide enough safety margin to not risk serious injury or death in operational conditions. However, as a scientist involved in the US programme has noted, compounds that are very potent tend to have low safety margins. If a compound has a wide safety margin (a high therapeutic index) it will tend to have a long onset time or not be sufficiently potent.<sup>303</sup> In fact, researchers at the Federation of American Scientists developed a model illustrating that even with a safety margin higher than any known sedative or anaesthetic drug a chemical used as an incapacitating agent would be expected to cause at least 10% fatalities.<sup>304</sup> Initially potent sedative and anaesthetic drugs were discounted as potential weapons due to their low safety margins and psychomimetic agents such as BZ were favoured. With changing operational requirements demanding very rapid incapacitation and the discovery of opioid agents with wider safety margins in the 1970's, namely the fentanyl analogues, attention again turned to these types of agent. However, these newer compounds still exhibited safety margins that were too low due to the major side effect of respiratory depression, which is particularly marked in primates. Efforts to militate against this fatal side effect led weapons developers to mix these agents (agonists) with antidotes This approach taken by US military researchers in the 1990's (antagonists). apparently succeeded in producing wider safety margins. And the strategy of mixing agonist and antagonist has continued to be investigated as a solution to the safety margin issue, for example by Russian researchers. Another strategy that has been proposed for reducing side effects and thereby increasing safety margins is employing different agents in combination to take advantage of synergistic effects that, for example, reduce the dose of a certain drug required to elicit the desired effect, thereby reducing the dose-dependent side effects. This is the approach been taken by Czech scientists in their current efforts to develop incapacitating agent weapons, which they claim will enable 'reversible immobilization.' Despite these attempted strategies, the problem of ensuring safety whilst retaining effectiveness does not appear to have been solved.<sup>305</sup>

The final major technical barrier to development of incapacitating agents is delivery. Inducing the level of incapacitation desired whilst preventing adverse effects requires careful control of the dose received especially with the types of agent under consideration, which tend to have low safety margins.<sup>306</sup> As Coupland has noted in relation to this issue, "...the only difference between a drug and a poison is the dose".<sup>307</sup> In a clinical setting the dose of an anaesthetic or sedative drug to be administered is precisely calculated according to body weight, age, and health and, furthermore, vital signs are continuously monitored. In their experiments to develop incapacitating agent weapons, Czech researchers calculated the doses in this way. Clearly in operational situations it is not possible to tailor the dose to each individual exposed. US military researchers have concentrated on delivery of agents as an aerosol for inhalation. Mears has argued that aerosol delivery provides greater safety because children, for example, have smaller lungs and therefore inhale a smaller dose.<sup>308</sup> However, this is a crude measure that does not take the other factors mentioned above into account nor the difficulties in predicting aerosol droplet dispersal inside a building let alone in the open air.<sup>309</sup> Moreover, there are the overarching problems of delivering an even concentration of the agent over a given area and cumulative intake of agent over time, which is even more pronounced in an enclosed space. As the researchers from the Federation of American Scientists have noted:

Where the concentration is higher, lethality will be greater; and where the concentration is lower, the agent will be less effective. The only practical way to maintain effectiveness in the face of uneven concentration is to use enough agent to guarantee that the minimal concentration in any area exceeds that needed to achieve effective incapacitation. However, this will mean that some areas will contain higher concentrations of the agent, enough to cause significant lethality.<sup>310</sup>

Police weapons developers have looked at projectiles that deliver the agent through the skin, but again it is not practical to tailor the dose to each individual targeted. Dart guns for intramuscular delivery have been ruled out as impractical due to risks of causing serious injury through hitting an unintended area and dangers of hitting a blood vessel, which could result in overdose. <sup>311</sup> Military delivery system development, on the other hand, has focused on delivery of chemical agents over long distances to be released as an aerosol or spray over a wide area to affect a group of people rather than an individual.

The technical barrier of delivery not been overcome and it seems inconceivable that the dose can be controlled beyond a certain extent through delivery system development alone. Therefore efforts are co-dependent on the aforementioned technical challenge of developing agents, mixtures of agents, or combinations of agents and antidotes which combine very high safety margins with sufficient potency. It is exactly this combination of technical advances that developers appear to be relying on.<sup>312</sup> Writing in 2003, one proponent claimed that such developments may be within the reach of ongoing secretive research efforts:

...remarkable progress has been made in the techniques to deliver immobilizing agents and in the development of safer, faster-acting potent compounds of extremely short duration in the last decade. Much of this work is either privileged or currently not available to the public and therefore unpublished.<sup>313</sup>

#### 1.5.2 Legal Constraints

Clearly a major factor affecting the development of biochemical incapacitating agents has been the emergence of international legal regimes governing chemical and biological weapons. According to the National Research Council panel on "non-lethal" weapons, the US military research and development of incapacitating agent weapons was halted in the early 1990's due to the negotiation of the Chemical Weapons Convention (CWC):

A significant program was conducted at Edgewood Arsenal, Aberdeen Proving Grounds, Maryland, on a spectrum of chemical systems for antimateriel and antipersonnel NLWs, such as *calmatives*, lachrimators, and malodorants. Specific details remain classified. The program, after many years of Army R&D investment and the identification of promising technologies, was concluded with adoption of the Chemical Weapons Convention in the early 1990s.<sup>314</sup> [emphasis added]

However, this respite was temporary and not all encompassing. Closely related research on incapacitating agents had continued to be sponsored by the National Institute of Justice and by the late 1990's the military programme itself had been revived. The Chemical Weapons Convention prohibits the development and use of any toxic chemical as a weapon. However, although it prohibits the use of riot control agents (irritant chemical weapons) as a "method of warfare", it permits their use for "law enforcement including domestic riot control".<sup>315</sup> Rather than limiting military interest in chemical weapons to irritant agents for use in specific circumstances such as civilian riot control, the US has pushed back against these restrictions in two interrelated ways. Firstly, the unique US position on riot control agents, meaning that they do not view them as chemical weapons and that their national policy on use contravenes the CWC in certain ways,<sup>316</sup> has been maintained with efforts by the Department of Defense to advocate widening of riot control agent use to warfare.<sup>317</sup> Secondly, the US has attempted to present incapacitating agents as "new" riot control agents despite their differences, and even suggested that incapacitating agents could be designed that better fit the definition of riot control agents.<sup>318</sup> The seeds for this strategy were sown during the negotiation of the Chemical Weapons Convention when ambiguities in the text were secured that left room for differing interpretations.<sup>319</sup>

The UK Northern Ireland Office has noted that the prohibition on the use of riot control agents in warfare serves to provide legal obstacles to countries that want to develop inappropriate agents as riot control agents and inappropriate delivery systems for riot control agents, such as mortar and artillery rounds.<sup>320</sup> However, this has not prevented the US military from pursuing this exact strategy. In a 2000 report of US/UK wargaming on "non-lethal" weapons the US has gone so far as to say that:

 $\dots$  a research and development program with respect to  $\dots$  chemically based calmatives as an RCA [riot control agent]  $\dots$  [will] be continued as long as it is cost-productive to do so.<sup>321</sup>

This desire to circumnavigate legal strictures appears to be driven by a conviction of the operational utility of biochemical incapacitating weapons for US military operations. The same 2000 report observed:

During the war game scenarios, numerous participants expressed the desire to have a NLW [non-lethal weapon] that could quickly incapacitate individuals with little or no after-effects. The participants desired this NLW to be employed in a variety of scenarios ranging from

crowd control to incapacitating enemy combatants. Generally, a chemically based calmative agent was viewed as the technology that could provide this capability.  $^{322}$ 

Of course, the use of chemical weapons for "incapacitating enemy combatants" would clearly violate the CWC. Nevertheless, the National Research Council argued that the military use of incapacitating agents in certain situations was not prohibited:

... it [the CWC] does not preclude such work or the employment of such agents in specified and increasingly important military situations, such as civilian crowd control in peacekeeping or humanitarian relief operations.<sup>323</sup>

And this leads to the central issue of "law enforcement" not being defined by the CWC, a problem in relation to emerging biochemical incapacitating weapons that was recognised long before the CWC came into force.<sup>324</sup> Dando has described it as follows:

 $\dots$  there is clearly a grey area where different interpretations of what is permitted are possible – when, in short, does law enforcement end and a method of warfare begin?<sup>325</sup>

Furthermore, there are differences of opinion on whether the CWC permits the use of any other chemical agents apart from riot control agents (i.e. irritant chemical weapons) for "law enforcement including domestic riot control". Krutzsch and others have argued that it does not,<sup>326</sup> whereas Fidler has argued that chemical agents permitted for these purposes are not limited to riot control agents.<sup>327</sup> He notes that this point of view is reinforced by the muted reaction by other States to the Russian use of incapacitating agents in Moscow in 2002. Indeed events in Moscow are likely to have increased interest in the development of incapacitating agents,<sup>328</sup> especially as the operation was considered a success amongst many observers including NATO's panel on "non-lethal" weapons.<sup>329</sup> In a 2006 paper expressing concerns over the development of these weapons Pearson observed:

Unfortunately, efforts to develop incapacitating biochemical weapons may well gather steam as more nations become intrigued by them and, observing the efforts of Russia and the United States, become convinced not only that effective and acceptably "non-lethal" incapacitating agents can be found, but that their use will be legitimized.<sup>330</sup>

This "creeping legitimization" of new biochemical weapons, as described by Perry Robinson,<sup>331</sup> is seen as the greatest threat to the existing prohibitions on chemical and biological weapons by arms control researchers<sup>332</sup> and a contributing factor to what Wheelis and Dando have termed the imminent "militarization of biology". <sup>333</sup> However, the political response to the legal challenge presented by continued development of incapacitating agents has been complete avoidance of the issue. The First Review Conference of the Chemical Weapons Convention (CWC) in 2003 failed to address the topic, even with events of Moscow fresh in the memory, <sup>334</sup> and discussions in the context of the Biological Weapons Convention (BWC) have remained peripheral.<sup>335</sup> With the confluence of chemistry and biology brought about by an increasingly molecular basis of understanding life processes, the relevance of the BWC to this issue has been emphasised.<sup>336</sup> There is no exemption in the BWC akin to the CWC's "law enforcement" provision.<sup>337</sup> Naturally occurring bioregulators and toxins are covered by the BWC as well as their synthetic chemical analogues (i.e. drugs) that bind to the same receptor sites in the body.<sup>338</sup> Nevertheless, even naturally occurring bioregulators have been put forward as potential incapacitating agents.<sup>339</sup>

All the while others in related defence communities warn of the emergence of "advanced biological warfare agents" that may be "… rationally engineered to target specific human biological systems at the molecular level" having a variety of effects "… including death, incapacitation, neurological impairment." <sup>340</sup> Bioregulator-type agents are one potential class of advanced biological weapon, considered in the past as more potent replacements for classical chemical weapons.<sup>341</sup> A joint committee of the US Institute of Medicine and the National Research Council addressing 'Advances in Technology and the Prevention of Their Application to Next Generation Biowarfare Threats' also drew attention to the danger of bioregulator weapons.<sup>342</sup> The contradiction is glaring when biochemical weapons are promoted on the one hand as counter-terrorist weapons whilst warnings are issued of the very same class of weapons. The two are separated by the gulf in terminology: "non-lethal weapons" versus "weapons of mass destruction".

### 1.5.3 Advocacy

Another important factor affecting the development of these weapons has been advocacy. Furmanski's analysis of the development of biochemical incapacitating agents during the Cold War concluded:

One lesson is that the energy and commitment of advocacy has been overridingly important in the development or suppression of non-lethal agents when they are in the developmental stage. Critical to the success of an advocacy group is its access to the media, politicians and political organisations.<sup>343</sup>

One of the most prominent and well-connected US organisations addressing the issue of "non-lethal" weapons, and chemical weapons in particular, has been the Washington-based think-thank the Council on Foreign Relations (CFR). In their 1995 report on "non-lethal" weapons the CFR 'task force' acknowledged the CWC's prohibitions of chemical weapons but argued: "It would, of course, be a tragic irony if nations used lethal means against noncombatants because non-lethal means were banned by an international convention."<sup>344</sup> A follow up 'task force' report published in 1999 argued that: "On occasion, U.S. security might be improved by a modification to a treaty such as the Chemical Weapons Convention or the Biological Weapons Convention."<sup>345</sup> However, in a 2005 paper Fidler reflects on a "sea change" in opinion at the CFR illustrated in their most recent report from 2004.<sup>346</sup> With a realisation of the wider dangers associated with pursuing new biochemical weapons the CFR report concluded:

The Task Force believes that to press for an amendment to the CWC or even to assert a right to use RCAs as a method of warfare risks impairing the legitimacy of all NLW. This would also free others to openly and legitimately conduct focused governmental R&D that could more readily yield advanced lethal agents than improved nonlethal capabilities. ... Accordingly, the Task Force judges that on balance the best course for the United States is to reaffirm its commitment to the CWC and the BWC and to be a leader in ensuring that other nations comply with the treaties.<sup>347</sup>

Furthermore the CFR report even expressed doubt about the operational viability of military incapacitating agent weapons:

We note also that we have seen no full scenarios for the use of calmatives. What happens in a situation where, after everyone is confused or knocked out, they begin to revive, and the United States does not have an overwhelming presence?<sup>348</sup>

As was clear from the preface to the 2003 National Research Council (NRC) report on "non-lethal" weapons, the US State Department seems to concur with the concerns expressed by the CFR.<sup>349</sup> Nevertheless this message seems to receive scant attention at the Department of Defense (DOD), where advocates continue to argue against this position. The Defense Science Board (DSB), which advises the DOD on science and technology matters, has urged development of biochemical weapons regardless of the international legal prohibitions. A 1994 DSB report, *Military Operations in Built-up Areas*, argued:

... it seems reasonable to us that the U.S. should develop promising nonlethal chemical agents that can disperse crowds, calm rioters, or disable hostiles, and as a minimum, have select capabilities on hand *even though we may be prohibited from employing them*.<sup>350</sup> [emphasis added]

Ten years later, in a report addressing Future *Strategic Strike Forces* published during the same month as the most recent CFR report, the DSB recommended that: "Applications of biological, chemical or electromagnetic radiation effects on humans should be pursued."<sup>351</sup> In the section on "strategic payload concepts" the report notes:

- Calmatives might be considered to deal with otherwise difficult situations in which neutralizing individuals could enable ultimate mission success
- The principle technical issue is the balance between effectiveness (i.e., the targets are truly "calmed") and margins of safety (i.e., avoiding overexposure and resulting fatalities of neutral bystanders)
- The treaty implications are significant<sup>352</sup>

A 2004 NATO report, *Non-Lethal Weapons and Future Peace Enforcement Operations*, also listed incapacitating biochemical weapons amongst "technologies of interest".<sup>353</sup> Nevertheless, frustrations were evident at a 2005 conference on "non-lethal" weapons sponsored by the Joint Non-Lethal Weapons Directorate (JNLWD), where a military lawyer from the Office of the US Navy's Judge Advocate General (JAG) doubted the legality of biochemical incapacitating weapons for the military.<sup>354</sup> More recently, a 2006 paper published by the US Air War College argued for the US to reject the Chemical Weapons Convention (CWC) in order to enable the development and use of incapacitating biochemical weapons in the so called "global war on terrorism".<sup>355</sup>

An important element of advocacy has been that emanating from the institutions that are responsible for weapons research and development. With the growing opposition to "lethal" chemical weapons from World War I onwards, these institutions in the US sought to prioritise and promote "non-lethal" incapacitating agent development during the Cold War. And later, during the early 1990's following the negotiation of the Chemical Weapons Convention (CWC) and the curtailing of the Advanced Riot Control Agent Device (ARCAD) programme, scientists at the Army's Edgewood Research, Development, and Engineering Centre (ERDEC) sought to revive the programme by pointing to a perceived 'loophole' in the treaty language.<sup>356</sup> Later still, in 1997, the military's preliminary legal review of various chemical weapons conducted by the Navy's Judge Advocate General (JAG) at the request of the Joint

Non-Lethal Weapons Directorate (JNLWD) seemed to report with the intention of enhancing ambiguity to enable weapons development to proceed. <sup>357</sup> And subsequently the Department of Defense (DOD) made clear that it would find a way to pursue prohibited weapons development by subcontracting to the Department of Justice (DOJ) or the Department of Energy (DOE) if necessary.<sup>358</sup> In an editorial rueing the missed opportunity to address the issue of incapacitating agents at the First Review Conference of the CWC in 2003, Meselson and Perry Robinson made the point succinctly:

There is another kind of escalation, which is the fostering of the growth and influence of institutions that are dependent upon the development and weaponization of chemical agents. Such institutions and their associated bureaucracies and dependent communities inevitably become a source of pressure for doing more in this area, and for promoting the assimilation of chemical weapons into the structures and doctrine of state forces.<sup>359</sup>

### **1.5.4** The Role of Scientists

Another relevant factor has been the support and collaboration of scientists outside these dependent institutions. Many of these are medical doctors since weapons developers have sought to draw on expertise in anaesthesiology. For example, during the 1980's and 1990's the leading US anaesthesiologist Prof. Theodore Stanley of the University of Utah, who had been involved in advancing anaesthetic techniques such as new means of administering fentanyl for pain relief, had also collaborated on the development of biochemical incapacitating weapons. Following the events in Moscow, Stanley publicly expressed support for expanding the research and development of these weapons in the *European Journal of Anaesthesiology*, citing the need for these weapons in counter-terrorism operations.<sup>360</sup> In another paper in the *Annals of Emergency Medicine* three medical toxicologists expressed support for these weapons arguing:

The use of a "sleeping gas" or calmative agent in this setting is a novel attempt at saving the most lives. ... Greater collaboration between clinicians and military planners is encouraged.<sup>361</sup>

Similarly, the broad-brush issue of counter-terrorism is apparently a driver for the Czech anaesthetists currently collaborating on the development of these weapons. In their 2005 paper they argued:

...many agents used in everyday practice in anesthesiology can be employed as pharmacological non-lethal weapons. An anesthetist familiar with the pharmacokinetics and pharmacodynamics of these agents is thus familiar with this use. As a result, he or she can play a role in combating terrorism.<sup>362</sup>

Issues of medical ethics go unaddressed in these papers, the powerful combination of the "non-lethal" weapons moniker and the rhetoric of the so called "war on terror" apparently reducing the concerns that a doctor might have in collaborating with the development of drugs as weapons rather than as treatments. Others have raised concerns about these issues.<sup>363</sup> Coupland, for example, has pointed out that "… medical professionals could easily be caught in a spiral of weapon development and counter-measure."<sup>364</sup> At the time of writing the British Medical Association (BMA) Board of Science published a report entitled *The use of drugs as weapons*, which warned against ongoing weapons development efforts raising pharmacological, clinical, ethical and legal concerns.<sup>365</sup>

# 1.5.5 Public Opinion

Of course wider public opinion also influences the development of these weapons. For example, the exposure of the extensive human experimentation that occurred during the US Cold War programme led to increased scrutiny and subsequently restrictions on the human testing necessary for the development of new agents. As the international prohibitions of chemical and biological weapons have become normalised, so public opinion has tended to reflect these norms. The norms are reinforced by the overriding contemporary discourse of terrorism, which emphasises the "threat" of "weapons of mass destruction", chemical and biological weapons included. For these reasons developers of biochemical incapacitating weapons have sought to reframe them as somehow separate whilst carrying out research and In fact, the issue of secrecy may turn out to be development in secret. counterproductive in terms of garnering support for these weapons. During the Cold War programme, as Furmanski has observed, secrecy contributed to the lack of public and political support for incapacitating agents whilst the more open consideration of sensory irritant chemicals aided their acceptance.<sup>366</sup> Nevertheless, the softening and manipulation of language is a powerful tool. Under the overall "non-lethal" banner, chemical and biological agents have become "calmatives" and "weapons" have become "techniques" or "capabilities". Invoking the fear of terrorism, including chemical- and bio- terrorism, the development of these very weapons is then, paradoxically, presented as a practical counter-terrorism solution. Perhaps the tacit support of the US President and the UK Prime Minister of the use of biochemical weapons by Russian forces during the Moscow theatre siege is a measure of proponents' success in clouding the issue.<sup>367</sup>

# **1.6 Conclusion**

Clearly advances in science and technology since efforts to develop biochemical incapacitating weapons began in the early 1950's have lowered the bar considerably to achieving weapons developers longstanding goals. Significant technical barriers remain, however, that may prove insurmountable. Nevertheless, the perceived potential for a scientific solution has seemingly been sufficient to sustain continued weapons research and development. 368 The prohibitions of the 1993 Chemical Weapons Convention have slowed but not halted this process, which has been given renewed impetus by the contemporary focus on counter-terrorism and operational demand for "non-lethal" weapons. Moreover, the first large-scale use of these weapons in Moscow in 2002 and the results, which could not conceivably be described as "non-lethal", apparently proved generally acceptable to the international community at the time.<sup>369</sup> The continuing military and police interest in biochemical incapacitating weapons means that we now sit at the brink of wider proliferation, and the consequences that process entails, unless greater political attention can be brought to bear in strengthening the existing legal constraints on such weapons development.

<sup>&</sup>lt;sup>1</sup> Cooper, G. and Rice, P. (eds.) (2002) Chemical Casualties: Centrally acting incapacitants. *Journal of the Royal Army Medical Corps*, Vol. 148, No. 4, pp. 388-391; Also see: Stockholm International Peace Research Institute (SIPRI) (1973) *The Problem of Chemical and Biological Warfare. Volume II: CB Weapons Today.* Stockholm: Almqvist & Wiksell, pp. 302-303; US Army (1996) Part III, Chapter 6:

Incapacitatants. In: FM 8-9: NATO Handbook on the Medical Aspects of NBC Defensive Operations. AmedP-6(B). Washington, DC: US Army.

<sup>3</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory.

<sup>4</sup> This reflects an overall softening of language with the aim of gaining greater acceptance for new biochemical weapons.

<sup>5</sup> The terms 'incapacitating chemical' and incapacitating biochemical' will be used interchangeably in this paper to refer to this type of weapon; Kelle, A, Nixdorf, K. and Dando, M. (2006) *Controlling Biochemical Weapons: Adapting Multilateral Arms Control for the 21st Century*. New York: Palgrave Macmillan.

<sup>6</sup> Dando, M. (2002) Scientific and technological change and the future of the CWC: the problem of non-lethal weapons. *Disarmament Forum* [The CWC Review Conference], No. 4, pp. 33-44; Wheelis, M. and Dando, M. (2005) Neurobiology: A case study of the imminent militarization of biology. *International Review of the Red Cross*, No. 859, pp. 553-572.
 <sup>7</sup> Douglass Jr., J. (1988) Soviets Surge in Biochemical Warfare; West Remains Drugged with Apathy.

<sup>7</sup> Douglass Jr., J. (1988) Soviets Surge in Biochemical Warfare; West Remains Drugged with Apathy. *Armed Forces Journal International*, August 1988.

<sup>8</sup> Taken from the following reference where the title is "Chemical and Biological Weapons Spectrum": Pearson, G. (2002) Relevant Scientific And Technological Developments For The First CWC Review Conference: The BTWC Review Conference Experience. *CWC Review Conference Paper No.1*. Department of Peace Studies, University of Bradford.

<sup>9</sup> Department of Defense (1996) Advances in Biotechnology and Genetic Engineering: Implications for the Development of New Biological Warfare Agents. Washington, DC: Office of the Deputy Assistant Secretary of Defense for Chemical and Biological Defense, p. 4.

<sup>10</sup> Kagan, E. (2001) Bioregulators as Instruments of Terror. *Clinics in Laboratory Medicine*. Vol. 21, No. 3. pp. 607-18
 <sup>11</sup> Petro, J., Plasse, T. and McNulty, J. (2003) Biotechnology: Impact on Biological Warfare and

<sup>11</sup> Petro, J., Plasse, T. and McNulty, J. (2003) Biotechnology: Impact on Biological Warfare and Biodefense. *Biosecurity and Bioterrorism*, Vol. 1, No. 3, pp. 161-168; Stockholm International Peace Research Institute (SIPRI) (1973) *The Problem of Chemical and Biological Warfare*. *Volume II: CB Weapons Today*. Stockholm: Almqvist & Wiksell, p. 303.

<sup>12</sup> Stockholm International Peace Research Institute (SIPRI) (1973) *The Problem of Chemical and Biological Warfare. Volume II: CB Weapons Today.* Stockholm: Almqvist & Wiksell, pp. 298-300; Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique.* State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory.

<sup>13</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory. The Pennsylvania State University.

<sup>14</sup> Ketchum, J. and Sidell, F. (1997) Incapacitants. <u>In:</u> Sidell, F., Takafuji, E., and Franz, D. (eds.) *Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare*. Washington D.C.: Borden Institute, Walter Reed Army Medical Center, pp. 287-305; Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>15</sup> Stockholm International Peace Research Institute (SIPRI) (1971) *The Problem of Chemical and Biological Warfare. Volume I: The Rise of CB Weapons.* Stockholm: Almqvist & Wiksell, pp. 75-77.
 <sup>16</sup> The CIA programmes are not covered here. For more information see, for example: Marks, J. (1991) *The Search for the Manchurian Candidate": The CIA and Mind Control.* New York: Norton. (First edition 1979)

<sup>17</sup> Stockholm International Peace Research Institute (SIPRI) (1971) *The Problem of Chemical and Biological Warfare. Volume I: The Rise of CB Weapons.* Stockholm: Almqvist & Wiksell, p. 75

<sup>18</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251.

<sup>19</sup> Stockholm International Peace Research Institute (SIPRI) (1971) *The Problem of Chemical and Biological Warfare. Volume I: The Rise of CB Weapons.* Stockholm: Almqvist & Wiksell, p. 76. <sup>20</sup> *Ibid.*, pp. 198-199.

<sup>21</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251.

 $<sup>^{2}</sup>$  Ibid.

<sup>22</sup> Stockholm International Peace Research Institute (SIPRI) (1973) *The Problem of Chemical and Biological Warfare. Volume II: CB Weapons Today.* Stockholm: Almqvist & Wiksell, pp. 298-300.
 <sup>23</sup> Perry Robinson, J. (1967) Chemical Warfare. *Science Journal*, No. 4, pp. 33-40; Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>24</sup> Furmanski, M. (2005) Military Interest in Low-lethality Biochemical Agents: The Historical Interaction of Advocates, Experts, Pragmatists and Politicians. *Background Paper prepared for the Symposium on Incapacitating Biochemical Weapons: Scientific, Military Legal and Policy Perspectives and Prospects, Geneva, Switzerland, 11 June 2005.* 

<sup>25</sup> Stockholm International Peace Research Institute (SIPRI) (1973) *The Problem of Chemical and Biological Warfare. Volume II: CB Weapons Today.* Stockholm: Almqvist & Wiksell, p. 301.
 <sup>26</sup> Dando, M. (1996) *A New Form of Warfare: The Rise of Non-Lethal Weapons.* London: Brasseys, pp. 87-88.

<sup>27</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251.

<sup>28</sup> Ibid.

<sup>29</sup> Stockholm International Peace Research Institute (SIPRI) (1973) *The Problem of Chemical and Biological Warfare. Volume II: CB Weapons Today.* Stockholm: Almqvist & Wiksell, p. 301.
 <sup>30</sup> Stockholm International Peace Research Institute (SIPRI) (1971) *The Problem of Chemical and*

*Biological Warfare. Volume I: The Rise of CB Weapons.* Stockholm: Almqvist & Wiksell, p. 77. <sup>31</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945.* Cambridge: Harvard

University Press, pp. 236-251; Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>32</sup> Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>33</sup> Ketchum, J. and Sidell, F. (1997) Incapacitants. <u>In:</u> Sidell, F., Takafuji, E., and Franz, D. (eds.) *Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare*. Washington D.C.: Borden Institute, Walter Reed Army Medical Center, pp. 287-305

<sup>34</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251; Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5; At the time of writing a new book was published that details research and development of incapacitating agents at Edgewood Arsenal during the 1960's: Ketchum, J. (2007) *Chemical Warfare: Secrets Almost Forgotten*. James S. Ketchum, December 2006. Details available March 2007 at: <u>http://www.forgottensecrets.net/</u>

<sup>35</sup> Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>36</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251

<sup>37</sup> Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>38</sup> Pfizer and Co., Inc. (1964) *Research on New Chemical Incapacitating Agents. Army CRDC contract* #DA18-108-AMC-240(A). Annual Report No. 1. June 28, 1963 – June 30, 1964. Part I. Groton, CT: Pfizer and Co., Inc. Available March 2007 at: <u>http://www.thememoryhole.org/mil/cbr/pfizer-cw.htm</u> <sup>39</sup> Witten, B. (1968) *Nonlethal Agents in Crime and Riot Control*. Edgewood Arsenal Technical

Memorandum EATM 133-1. Chemical Research Laboratory, Edgewood Arsenal, US Army.

<sup>40</sup> *Ibid.*; Perry Robinson, J. (1994) Developments in "Non-Lethal Weapons" involving chemicals. <u>In:</u> International Committee of the Red Cross. *Report of the Expert Meeting on Certain Weapon Systems and on Implementation Mechanisms in International Law, Geneva, 30 May – 1 June 1994*. Geneva: International Committee of the Red Cross, pp. 92-97.

<sup>41</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251.

 $^{42}$  Ibid.

<sup>43</sup> Dando, M. (2006) *The UK's Search for an Incapacitating ('Non-Lethal') Chemical Agent in the 1960s.* Bradford Science and Technology Paper No. 6. Bradford: University of Bradford, Department of Peace Studies, Bradford Disarmament Research Centre. <sup>45</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251

<sup>46</sup> *Ibid.*, p. 243.

<sup>47</sup> Dando, M. (1996) *A New Form of Warfare: The Rise of Non-Lethal Weapons*. London: Brasseys, p. 147.

<sup>48</sup> *Ibid.*, p. 149.

<sup>49</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003.* Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October
2003, p. 68; Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>50</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

pp. 136-168

<sup>31</sup> Perry Robinson, J. (1994) Developments in "Non-Lethal Weapons" involving chemicals. <u>In:</u> International Committee of the Red Cross. *Report of the Expert Meeting on Certain Weapon Systems and on Implementation Mechanisms in International Law, Geneva, 30 May – 1 June 1994*. Geneva: International Committee of the Red Cross, pp. 92-97.

<sup>52</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, pp. 236-251; Kirby, R. (2006) Paradise Lost: The Psycho Agents. *The CBW Conventions Bulletin*, No. 71, pp. 1-5.

<sup>53</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

<sup>54</sup> Dando, M. and Furmanski, M. (2006) Midspectrum Incapacitant Programs. <u>In:</u> Wheelis, M., Rózsa, L., and Dando, M. (Eds). *Deadly Cultures: Biological Weapons Since 1945*. Cambridge: Harvard University Press, p. 245.

<sup>55</sup> Dando, M. (1996) A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, p. 140.

<sup>56</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003.* Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 71-72.

<sup>57</sup> *Ibid.*, p. 73.

<sup>58</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

<sup>59</sup> Ibid.

<sup>60</sup> Dando, M. (1996) *A New Form of Warfare: The Rise of Non-Lethal Weapons*. London: Brasseys, p. 147.

<sup>61</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168; Perry Robinson, J. (2003) Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003. Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003.

<sup>62</sup> Harvard Sussex Program (2003) Editorial: 'Non-Lethal' Weapons, the CWC and the BWC. *The CBW Conventions Bulletin*, No. 61, pp. 1-2.

<sup>63</sup> Schulz, W. (2005) Top Pharmaceuticals: Fentanyl. Chemical and Engineering News. Special Issue, Vol. 83, Issue 25. Available March 2007 at:

http://pubs.acs.org/cen/coverstory/83/8325/8325fentanyl.html

 <sup>64</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events,* 1945-2003. Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 92.

<sup>65</sup> CRDEC was renamed Edgewood Research, Development, and Engineering Center (ERDEC) in the early 1990's.

<sup>66</sup> Mears, K. (1999) *Nonlethal Chemical Incapacitants*. Thesis, CSC. Quantico, VA: Marine Corps University.

<sup>67</sup> Stanley, T. (2003) Human immobilization: is the experience in Moscow just the beginning? *European Journal of Anaesthesiology*. Vol. 20, No. 6, pp. 427-428.

<sup>68</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

Bradford Science and Technology Report No. 8, August 2007.

<sup>&</sup>lt;sup>44</sup> Ibid.

 <sup>69</sup> Hart, S. (2002) Statement before The Subcommittee on Aviation, Committee on Transportation and Infrastructure, U.S. House of Representatives. Washington, DC: US House of Representatives.
 <sup>70</sup> Funding was \$500,000 in 1989 and \$580,000 in 1990: Pilant, L. (1993) Less-than-Lethal Weapons: New Solutions for Law Enforcement. Science and Technology, Washington D.C.: International Association of Chiefs of Police, December 1993; Seaskate, Inc. (1998) The Evolution and Development of Police Technology. A Technical Report prepared for The National Committee on Criminal Justice Technology, National Institute of Justice, Grant No.: 95-IJ-CX-K001(S-3). Washington, DC: Department of Justice, National Institute of Justice, p. 44.

<sup>71</sup> Hart, S. (2002) Statement before The Subcommittee on Aviation, Committee on Transportation and Infrastructure, U.S. House of Representatives. Washington, DC: US House of Representatives.

<sup>72</sup> Pilant, L. (1993) Less-than-Lethal Weapons: New Solutions for Law Enforcement. *Science and Technology*, Washington D.C.: International Association of Chiefs of Police, December 1993; Seaskate, Inc. (1998) *The Evolution and Development of Police Technology*. A Technical Report prepared for The National Committee on Criminal Justice Technology, National Institute of Justice, Grant No.: 95-IJ-CX-K001(S-3). Washington, DC: Department of Justice, National Institute of Justice, p. 44.

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<sup>74</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

<sup>75</sup> Perry Robinson, J. (1994) Developments in "Non-Lethal Weapons" involving chemicals. <u>In:</u> International Committee of the Red Cross. *Report of the Expert Meeting on Certain Weapon Systems and on Implementation Mechanisms in International Law, Geneva, 30 May – 1 June 1994.* Geneva: International Committee of the Red Cross, pp. 92-97.

<sup>76</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003.* Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 17.

<sup>77</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

 <sup>78</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events,* 1945-2003. Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 84.

<sup>79</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168; Perry Robinson, J. (2003) Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003. Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 84-85.

<sup>80</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events,* 1945-2003. Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 95.

<sup>81</sup> Pearce, H. (1994) *Demonstration of Chemical Immobilizers*. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>82</sup> United Nations (1993) Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction. Opened for signature on 13 January 1993, Paris.

<sup>83</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168.

<sup>84</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003.* Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 92.

<sup>85</sup> Dando, M. (1996) A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 164-165.

<sup>86</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003.* Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 78; Dando, M. (1996) *A New Form of Warfare: The Rise of Non-Lethal Weapons.* London: Brasseys, pp. 160-163.

<sup>87</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. *A New Form of Warfare: The Rise of Non-Lethal Weapons*. London: Brasseys, pp. 136-168; Vainio, O. (1989) Introduction to the clinical pharmacology of medetomidine. *Acta Veterinaria Scandinavica*, Supplement, Vol. 85, pp. 85-88. Suppl. 1989;85:85-8.

<sup>88</sup> Dando, M. (1996) An Assault on the Brain? <u>In:</u> Dando, M. A New Form of Warfare: The Rise of Non-Lethal Weapons. London: Brasseys, pp. 136-168

<sup>89</sup> Edgewood ERDEC (1989-94) Scientific Conference on Chemical and Biological Defense Research: Abstract Digest. Aberdeen Proving Ground, MD: US Army Chemical and Biological Defense Command. <u>Quoted in</u>: Dando, M. (1996) *A New Form of Warfare: The Rise of Non-Lethal Weapons*. London: Brasseys, p. 162.

<sup>90</sup> These documents were not publicly available until late 2003 following a Freedom of Information Act request by The Sunshine Project, a US Non Governmental Organisation working on chemical and biological weapons issues.

<sup>91</sup> Pearce, H. (1994) *Demonstration of Chemical Immobilizers*. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>92</sup> Ibid.

<sup>93</sup> Ferguson, C. P. (1994) Antipersonnel Chemical Immobilizers: Synthetic Opioids. Research proposal,
 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and
 Engineering Center.

<sup>94</sup> Ferguson, C. P. (1994) Antipersonnel Chemical Immobilizers: Sedatives. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>95</sup> Ferguson, C. P. (1994) Antipersonnel Chemical Immobilizers: Synthetic Opioids. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>96</sup> United States Patent Office (1998) *Opiate analgesic formulation with improved safety, United States Patent 5,834,477, 10 November 1998*; Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003*. Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 105.

<sup>97</sup> Pearson, A. (2006) Incapacitating Biochemical Weapons: Science, Technology, and Policy for the 21st Century. *The Nonproliferation Review*, Vol. 13, No. 2, July 2006, pp. 151-188; Stanley, T. (2000) Anesthesia for the 21st century. *Proceedings of Baylor University Medical Center*, Vol. 13, No. 1, pp. 7-10.

<sup>98</sup> Ferguson, C. P. (1994) Antipersonnel Chemical Immobilizers: Synthetic Opioids. Research proposal,
 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and
 Engineering Center.

<sup>99</sup> *Ibid*.

<sup>100</sup> Ferguson, C. P. (1994) *Antipersonnel Chemical Immobilizers: Sedatives*. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>101</sup> *Ibid*.

<sup>102</sup> Ferguson, C. P. (1994) *Antipersonnel Calmative Agents*. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>103</sup> Ferguson still holds this view as seen in: Davison, N. and Lewer, N. (2004) *Bradford Non-Lethal Weapons Research Project (BNLWRP) Research Report No. 5.* Bradford: University of Bradford, Department of Peace Studies, pp. 39-41; However, in recent years the term "calmative" has been used by weapons developers as a catch-all description for incapacitating agents.

<sup>164</sup> Ferguson, C. P. (1994) *Antipersonnel Calmative Agents*. Research proposal, 27 April 1994. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center.

<sup>105</sup> Stanley, T. (2000) Anesthesia for the 21st century. *Proceedings of Baylor University Medical Center*, Vol. 13, No. 1, pp. 7-10; Also see University of Utah Department of Anesthesiology faculty web page, available March 2007 at: <u>http://anesthesia.med.utah.edu/postgrad/faculty.htm</u>

<sup>106</sup> Perry Robinson, J. (2003) *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003.* Harvard-Sussex Program, University of Sussex, unpublished, version dated 8 October 2003, p. 108.

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<sup>108</sup> Pilant, L. (1993) Less-than-Lethal Weapons: New Solutions for Law Enforcement. Science and Technology, Washington D.C.: International Association of Chiefs of Police, December 1993

<sup>109</sup> Andresen, B. and Grant, P. (1997) Dose Safety Margin Enhancement for Chemical Incapacitation and Less-than-Lethal Targeting. NIJ Final Report and Recommendations. Livermore, CA: Lawrence Livermore National Laboratory, Nonproliferation, Arms Control, and International Security Directorate, Forensic Science Center R-Division, January 1997; This report was not publicly available until 2003 when obtained by The Sunshine Project under the Freedom of Information Act. <sup>110</sup> *Ibid.*, p. 2

<sup>111</sup> *Ibid.*, p. 2

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<sup>114</sup> *Ibid.*, p. 14.

<sup>115</sup> *Ibid.*, p. 6.

<sup>116</sup> *Ibid.*, p. 14.

<sup>117</sup> *Ibid.*, p. 16.

<sup>118</sup> *Ibid.*, p. 18.

<sup>119</sup> *Ibid.*, p. 20.

<sup>120</sup> Ibid., p. 20-21. <sup>121</sup> *Ibid.*, p. 21.

<sup>122</sup> *Ibid.*, p. 25.

<sup>123</sup> *Ibid.*, pp. 24-27.

<sup>124</sup> US Navy (1997) Preliminary Legal Review of Proposed Chemical-Based Nonlethal Weapons. Department of the Navy, Office of the Judge Advocate General, International & Operational Law Division. Available March 2007 at:

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<sup>125</sup> Department of Defense (1999) Chemical and Biological Defense Program. Topic #: CBD00-108: Chemical Immobilizing Agents for Non-Lethal Applications. Small Business Innovation Research Solicitation, Fiscal Year 2000. Washington, DC: Department of Defense. Available March 2007 at: http://www.acq.osd.mil/osbp/sbir/solicitations/sbir001/cbd001.htm <sup>126</sup> Ibid.

<sup>127</sup> *Ibid*.

<sup>128</sup> Edgewood Chemical Biological Center (2000) CB Quarterly, Issue No. 21, March 2000. Aberdeen Proving Ground, MD: US Army, Edgewood Chemical Biological Center, p. 19.

<sup>129</sup> Edgewood Chemical Biological Center (2000) CB Quarterly, Issue No. 22, June 2000. Aberdeen Proving Ground, MD: US Army, Edgewood Chemical Biological Center; Also see the OptiMetrics, Inc. web site available March 2007 at: http://optimetrics.org/

<sup>130</sup> Department of Defense (1999) Chemical and Biological Defense Program. Topic #: CBD00-108: Chemical Immobilizing Agents for Non-Lethal Applications. Small Business Innovation Research, Phase I Selections from the 00.1 Solicitation, Fiscal Year 2000, Washington, DC: Department of Defense. Available March 2007 at: http://www.dodsbir.net/selections/abs001CBD.htm

<sup>131</sup> i.e. considerably less than the \$1.25 million requested for the Phase I research in 1994.

<sup>132</sup> Regan, M. (2004) Marines Get Site to Pull Knockout Gas Info. Associated Press, 17 July 2004. Available March 2007 at: http://www.fas.org/sgp/news/2004/07/ap071704.html

<sup>133</sup> Ruppe, D. (2002) United States: U.S. Military Studying Nonlethal Chemicals. *Global Security* Newswire, 4 November 2002. Available March 2007 at:

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<sup>134</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory; Although this document was not classified it was not made publicly available until mid-2002 when it was obtained under a Freedom of Information Act request by The Sunshine Project. The INLDT subsequently published the document on their website a

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few months later with a minor adjustment to the front cover, removing a diagram of the fentanyl molecule and adding a preface to the report.

<sup>135</sup> *Ibid.*, p. 5.

<sup>136</sup> *Ibid.*, p. 7.

<sup>137</sup> Allison, G., Kelley, P., and Garwin, R. (2004) Nonlethal Weapons and Capabilities: Report of an Independent Task Force Sponsored by the Council on Foreign Relations. New York: Council on Foreign Relations, p. 2.

<sup>138</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory, pp. 9-10.

<sup>139</sup> *Ibid.*, p. 10.

<sup>140</sup> *Ibid.*, p. 10.

<sup>141</sup> *Ibid.*, p. 10.

<sup>142</sup> *Ibid.*, pp. 8-9; Over 7,800 references were complied into a database termed CALMATIVE, and a subsidiary database of subtopics and themes, termed CALMTOPICS, was also compiled. Neither of these are publicly available.

<sup>143</sup> Listed in the order agents are considered in the report. It is not clear whether this has any significance in terms of priorities.

 <sup>144</sup> Another characteristic noted in the report is that carfentanil has a long duration of action.
 <sup>145</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) *The Advantages and Limitations of* Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory, p. 33.

<sup>146</sup> Mears, K. (1999) Nonlethal Chemical Incapacitants. Thesis, CSC. Quantico, VA: Marine Corps University.

<sup>147</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory, p. 17. <sup>148</sup> *Ibid.*, p. 18.

<sup>149</sup> *Ibid.*, p. 19.

<sup>150</sup> Ibid., pp. 20-21; Gertler, R., Brown, H.C., Mitchell, D., and Silvius, E. (2001) Dexmedetomidine: a novel sedative-analgesic agent. Proceedings of Baylor University Medical Center, Vol. 14, No. 1, pp. 13-21.

<sup>151</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory, p. 21.

<sup>152</sup> One effect of dexmedetomidine is to increase the individuals' susceptibility to electric shock. The report points to the possibility of using this drug in association with electrical or electromagnetic "nonlethal" weapons.

<sup>153</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory, p. 21.

<sup>154</sup> *Ibid.*, p. 37. <sup>155</sup> *Ibid.*, p. 38. <sup>156</sup> *Ibid.*, p. 38. <sup>157</sup> *Ibid.*, pp. 21-25. <sup>158</sup> *Ibid.*, pp. 26-28. <sup>159</sup> *Ibid.*, p. 30. <sup>160</sup> *Ibid.*, p. 30. <sup>161</sup> *Ibid.*, pp. 28-31. <sup>162</sup> *Ibid.*, pp. 39-42.

<sup>163</sup> *Ibid.*, pp. 42-45. <sup>164</sup> *Ibid.*, p. 45.

<sup>165</sup> *Ibid.*, p. 46.

<sup>166</sup> *Ibid.*, pp. 47-48.

<sup>167</sup> *Ibid.*, p. 49.

<sup>168</sup> *Ibid.*, p. 6.

<sup>169</sup> *Ibid.*, p. 6; Stanley, T. (2003) Human immobilization: is the experience in Moscow just the beginning? European Journal of Anaesthesiology. Vol. 20, No. 6, pp. 427-428.

<sup>170</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory, Preface.

<sup>171</sup> The Sunshine Project (2002) *The MCRU Calmatives Study and JNLWD: A Summary of (Public) Facts.* The Sunshine Project, 19 September 2002. Available March 2007 at: <u>http://www.sunshine-project.org/incapacitants/mcrucalmfacts.html</u>
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<sup>173</sup> National Research Council (2003) An Assessment of Non-Lethal Weapons Science and Technology. Washington, DC: National Academies Press, pp. 43-44.

<sup>174</sup> Copeland, R. (2002) Joint Non-Lethal Weapons Program. Presentation to the 2002 Mines, Demolition and Non-Lethal Conference & Exhibition, 3-5 June 2002, National Defense Industrial Association (NDIA), US.

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<sup>178</sup> *Ibid.*, pp. 106-107.

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project.org/incapacitants/jnlwdpdf/usukassess.pdf <sup>180</sup> National Institute of Justice Grant No. 2001-RD-CX-K002. Details from NIJ Research Portfolio available December 2006 at: <u>http://nij.ncjrs.org/portfolio/</u> [Note, March 2007: This resource in no longer publicly available, it now appears to be password protected.].

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<sup>229</sup> *Ibid.*, p. 129.

<sup>230</sup> US/UK Non-Lethal Weapons Wargaming Program, US Marine Corps web site available June 2007 at: <u>http://www.wargaming.quantico.usmc.mil/programs/NLW/index.asp</u>

<sup>231</sup> House of Commons (2001) Non-lethal weapons, House of Commons Hansard Written Answers for 10 Apr 2001 (pt 9). London: HMSO, House of Commons Hansard.

 <sup>232</sup> United States/United Kingdom (2001) US/UK Non-Lethal Weapons (NLW)/Urban Operations Executive Seminar, 30 November 2000, London. Assessment Report. ONR-NLW-038.
 <sup>233</sup> Allison, G., Kelley, P., and Garwin, R. (2004) Nonlethal Weapons and Capabilities: Report of an

<sup>233</sup> Allison, G., Kelley, P., and Garwin, R. (2004) *Nonlethal Weapons and Capabilities: Report of an Independent Task Force Sponsored by the Council on Foreign Relations.* New York: Council on Foreign Relations, p. 26, "What is sought in this regard is the ability to send out in a discriminating fashion, preferably semi-automatically, containers with multiple rubber balls, dye cartridges, or whatever is in use, so that they will explode at a specified height above the crowd and project the NLW as desired. To clear a large crowd in other than combat situations, tear gas would also be a tool of choice, and such submunition systems would be helpful in that case as well as in the comparable domestic riot control actions."

<sup>234</sup> National Research Council (2003) *An Assessment of Non-Lethal Weapons Science and Technology*. Washington, DC: National Academies Press, p. 107.

<sup>235</sup> The Sunshine Project (2002) US Military Operating a Secret Chemical Weapons Program. The Sunshine Project News Release, 24 September 2002. Available March 2007 at: <u>http://www.sunshine-project.org/publications/pr/pr240902.html</u>
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<sup>239</sup> Vanek Prototype Co. (2002) Proposal for Multi-Shot Launcher with Advanced Less-Than-Lethal Ring Airfoil Projectiles. Submitted by Vanek Prototype Co. (2002-90-CA-IZ) to the US National Institute of Justice, 25 March 2002. Available March 2007 at: <u>http://www.sunshine-project.org/incapacitants/jnlwdpdf/dojrap.pdf</u>
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<sup>242</sup> Joint Non-Lethal Weapons Directorate (1999) *Joint Non Lethal Weapons Program News*, Vol. 2, No. 2, February 1999.

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<sup>244</sup> Primex Aerospace Company (2000) Overhead Liquid Dispersal System (OLDS) Non-Lethal Demonstration Program. DAAE30-99-C-1072. Final Report. 19 April 2000. Redmond, WA: Primex Aerospace Company. Available March 2007 at: http://www.sunshineproject.org/incapacitants/jnlwdpdf/primexolds.pdf <sup>245</sup> US Army (2001) Liquid Payload Dispensing Concept Studies Techniques for the 81mm Non-Lethal

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<sup>246</sup> Hegarty, R. (2003) Joint Non-Lethal Weapons Program: Non-Lethal Mortar Cartridge (NLMC). Presentation to the 2003 Picatinny Chapter/PEO Mortars Conference, National Defense Industrial Association (NDIA), US, 1-3 October 2003.

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<sup>260</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory.

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<sup>273</sup> United States Patent Office (2003) Rifle-launched non-lethal cargo dispenser, United States Patent 6,523,478, 25 February 2003.

<sup>274</sup> The Sunshine Project (2003) US Army Patents Biological Weapons Delivery System, Violates Bioweapons Convention. The Sunshine Project News Release, 8 May 2003.

<sup>275</sup> "A divisional patent application is an application claiming priority from some previously filed patent application (called a "parent application") in which more than one invention was disclosed. The divisional application has claims directed to a different invention than that claimed in the parent application. The most common way that this happens is that the Patent Office rules that your application contains more than one invention, communicating this in what is called a "restriction requirement". The applicant then elects to pursue one of the inventions in that application (the "parent application"), and optionally submits a "divisional application" containing the claims regarding another of the inventions." [From: http://research.hsc.unt.edu/ip\_terminology.html]

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<sup>293</sup> Advanced Polymer Laboratory (2003) Current Projects. APL, University of New Hampshire web site. Accessed November 2003 at: <u>http://www.unh.edu/apl/curentprojects.htm</u>; US Army (1997) Odorous Substances [redacted]. Research Proposal, July 1997. Aberdeen Proving Ground, MD: US Army Edgewood Research, Development, and Engineering Center. Available March 2007 at: <u>http://www.sunshine-project.org/incapacitants/jnlwdpdf/edgesmells.pdf</u>

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<sup>298</sup> Dando, M. (2002) Scientific and technological change and the future of the CWC: the problem of non-lethal weapons. *Disarmament Forum*. No. 4, pp. 33-44.

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<sup>304</sup> Klotz, L., Furmanski, M., Wheelis, M. (2003) *Beware the Siren's Song: Why "Non-Lethal" Incapacitating Chemical Agents are Lethal.* Washington D.C.: Federation of American Scientists (FAS); In Moscow the fatality rate was over 15%.

<sup>305</sup> Ruppe, D. (2002) United States I: New Research Offers Safer Incapacitating Chemicals. Global Security Newswire, 6 November 2002. Available March 2007 at:

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<sup>307</sup> Davison, N. and Lewer, N. (2004) *Bradford Non-Lethal Weapons Research Project (BNLWRP) Research Report No. 5.* Bradford: University of Bradford, Department of Peace Studies, pp. 35-38.

<sup>308</sup> Mears, K. (1999) *Nonlethal Chemical Incapacitants*. Thesis, CSC. Quantico, VA: Marine Corps University.

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<sup>310</sup> Federation of American Scientists Working Group on Biological Weapons (2003) *Position Paper: Chemical Incapacitating Weapons Are Not Non-Lethal.* Washington D.C.: Federation of American Scientists (FAS).

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<sup>312</sup> Lakoski, J., Bosseau Murray, W., and Kenny, J. (2000) *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*. State College, PA: Pennsylvania State University, College of Medicine & Applied Research Laboratory.
 <sup>313</sup> Stanley, T. (2003) Human immobilization: is the experience in Moscow just the beginning?

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<sup>315</sup> United Nations (1993) Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction. Opened for signature on 13 January 1993, Paris.

<sup>316</sup> Two of the provisions in US Executive Order 11850 (1975) – use of riot control agents against combatants employing civilians as human shields, and use against combatants attempting to capture

<sup>&</sup>lt;sup>295</sup> National Research Council (2003) An Assessment of Non-Lethal Weapons Science and Technology. Washington, DC: National Academies Press, p. 107.

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<sup>318</sup> United States/United Kingdom (2001) US/UK Non-Lethal Weapons (NLW)/Urban Operations Executive Seminar, 30 November 2000, London. Assessment Report. ONR-NLW-038; US Navy (1997) Preliminary Legal Review of Proposed Chemical-Based Nonlethal Weapons. Department of the Navy, Office of the Judge Advocate General, International & Operational Law Division; Riot control agents are defined in the Chemical Weapons Convention as those agents that "...can produce rapidly in humans sensory irritation or disabling physical effects which disappear within a short time following termination of exposure."

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<sup>323</sup> National Research Council (2003) An Assessment of Non-Lethal Weapons Science and Technology. Washington, DC: National Academies Press, p. 6.

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<sup>325</sup> Dando, M. (2002) Scientific and technological change and the future of the CWC: the problem of non-lethal weapons. *Disarmament Forum*. No. 4, pp. 33-44.

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