



EVALUATION OF INJECTION TECHNOLOGIES

Informal Meeting, Washington D.C., 16/17 November 1987
 Expanded Programme on Immunization

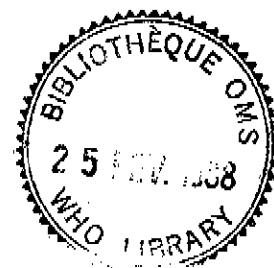
Summary Report

This was the second meeting of a group of WHO advisors to review the proposals of industry and inventors on the development of injection technologies to minimize the risk of cross infection. The method and the objectives of the review were the same as for the previous meeting (report presented as Annex).

A total of 37 submissions were received, 9 of which were modifications of those received in July but, at that time, were found to be not acceptable. A breakdown of these submissions, together with their major characteristics, their resource demands and their inactivation methods appears in Figure 1, and their current timetables are presented in Figure 2.

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Results of the meeting:

A progress report was made to the review group on 5 technologies which had been endorsed during or following the last EPITECH meeting in July (identified in Figure 1, column 3). One auto-destruct syringe and one pre-filled device are being developed by consulting engineers to USAID. Prototype samples of both of these devices are being manufactured by sub-contractors to the consulting engineers for field studies early in 1988. Manufacturers for quantity production of the two devices, should field studies prove successful, have not yet been identified.

A second auto-destruct syringe and a second pre-filled device are being developed by established manufacturers and production samples will be available for field studies in the first quarter of 1988. Quantity production of the pre-filled device is possible with only a short delay because similar devices are already manufactured for dentistry and for the military.

A fluid path blocking system developed by a university which, at the last meeting was considered by the Group to be highly promising, has made little progress because a source of funds for the research work involved has not been identified. The Group again recommended that this development be fully supported at the earliest opportunity. It is believed that the system could be incorporated into other auto-destruct syringes and prefilled devices as a backup to other methods of inactivation as it is virtually tamper-proof and could apparently be made available at very low cost.

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Figure 2 : TIMETABLES PROPOSED IN THE SUBMISSIONS

TIMETABLE Samples for field trial <<<<																									
Prepare for production >>>>																									
Ref. code	1987 Dec	1988 Jan	1988 Feb	1988 Mar	1988 Apr	1988 May	1988 Jun	1988 Jul	1988 Aug	1988 Sep	1988 Oct	1988 Nov	1988 Dec	1989 Jan	1989 Feb	1989 Mar	1989 Apr	1989 May	1989 Jun	1989 Jul	1989 Aug	1989 Sep	1989 Oct	1989 Nov	1989 Dec
Auto-destruct syringes:																									
A																									
B			<<<<	<<	FIELD TRIAL	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
C			<<	FIELD TRIAL	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
D			<<<<	<<<	FIELD TRIAL																				
E																									
F																									
G			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
H			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIALS	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
I			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIALS	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
J			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
K			<<<<	<<<<	<<<<	FIELD TRIAL																			
L			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL																
M			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIALS																
N			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIALS	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
O																									
P																									
Q																									
R																									
S			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL											
Pre-filled injection devices																									
T			<<<<	<<	FIELD TRIAL																				
U			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>	>>>>
V			<<<<	<<	FIELD TRIAL																				
W			<<<<	<<<<	<<	FIELD TRIAL																			
X																									
Y			<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL											
Z																									
AA																									
AB																									
AC																									
AD																									
AE			<<<<	<<	FIELD TRIAL																				
Jet injectors																									
AF			<<<<	<<<<	<<<<	<<<<	<<<<	FIELD TRIAL																	
Other relevant devices																									
AG			(PD p:																						
AH			(Bl.f:																						
AI			(Anti:																						
AJ			(Anti:																						
AK			(Need:																						

Thirty-two new or modified proposals were submitted to the Group for consideration. Two of these were considered by the Group to be sufficiently important to receive the necessary financial support and encouragement of WHO and UNICEF to develop and field test the device. Eight other proposals requiring additional development work or a level of funding which is not directly available from WHO, UNICEF or USAID at this time, were also considered by the Group to be sufficiently promising to progress to the stage of field studies.

The remaining proposals were either considered not to meet the requirements of the EPI or insufficient information had been provided to enable the Group to comprehend and evaluate the technology. These proposals were split into those for which WHO and UNICEF would welcome further correspondence and those which do not appear to merit further discussion.

WHO and UNICEF will not actively solicit new proposals for auto-destruct injection devices with needles again, unless progress on the current developments slows to an unacceptable level. However, the agencies will continue to review proposals of this type on an ad hoc basis if and when they are received. Work will continue, however, on the definition of requirements for low-workload jet injectors and a solicitation may be made by the agencies early in 1988.

Discussion:

Features which automatically protect against accidental wounding by an exposed needle (anti-stick features) are being increasingly incorporated into auto-destruct syringes and prefilled injection devices. The Group considered whether these features, which are included in the specifications of industrialized countries (notably the Ministry of Health, UK), should also be adopted for the EPI.

The Group concluded that, if anti-stick features could be added to current designs in an acceptable way, at a fractional extra cost and without adding to the training burden, they should be encouraged and evaluated in the field. Discussion took place on the relative merits of having the needle sheathed at all times and the desirability of keeping the needle in sight to determine the depth of penetration.

Until these points are made clear, passive anti-stick measures continue to be recommended for the EPI, including:

- re-sheathing needles with one hand only (using needle re-sheathing blocks) and/or,
- disposing of the syringe-needle combination in a specially designed disposal container.

It was noted by the Group that needle and syringe clipper devices become infected themselves and risk aerosol or splatter infection of the users. Unless such devices can be effectively sterilized, it was recommended that the needle be resheathed after use and/or dropped into a closed disposal container directly after use.

Several auto-destruct concepts now appear to allow for conventional aspiration of vaccine into the syringe and aspiration for presence of blood. One design even ensures that a full, rather than a partial, dose of vaccine is drawn into the syringe before injection. If these concepts prove to be practical and require little or no training, it appeared unlikely to the Group that other designs which limit or modify standard procedures will prove to be acceptable in the field.

For this reason, it was decided to allow only one model of syringe which requires pressure filling and which cannot aspirate for blood in the initial field studies. If these changes to current technique are found acceptable, studies of similar syringes may follow.

A number of concepts for pre-filled injection devices incorporated types of glass vial already available on the market. In spite of the immediate availability of this technology and the absence of the vaccine compatibility questions associated with storage of vaccine in plastic containers, the cost estimates even for a mass market have been high. (See technologies in Figure 1 which are marked 'YES' in the column indicating vaccine in a glass vial.)

By contrast, some cost estimates for plastic pre-filled devices have been low, particularly for those concepts which separate the vaccine storage container from the device which injects it. These containers appear to be more compact to store in the cold chain than self-contained injection devices. A suggestion from members of the Group was that the plastic vaccine containers might be standardized while a variety of injector devices could be made available to the field by different device manufacturers.

Whether this suggestion is accepted or not, it was foreseen that it will be necessary to standardize vaccine presentation for pre-filled devices in order that vaccine manufacturers continue to participate in the world market on an equivalent basis as they do today. It was, however, considered premature by the Group to make decisions on standardization before a range of pre-filled devices have been tried and evaluated in the field.

Although only a single low-workload jet injector was presented to the meeting for review and no formal solicitation has yet been made to the industry, several members of the group were of the opinion that great potential exists in the concept of a needle-less injector for avoiding the risks of cross infection and for simplifying the process of immunization. This opinion was expressed in spite of a general awareness of the maintenance and energy supplies which are commonly demanded by jet injection systems. It was agreed that an evaluation of the newly available jet injector is a high priority and that, if favorable, efforts should be renewed to develop performance requirements prior to a solicitation to industry.

A study of the impact of new injection technologies on the cost of the EPI, conducted by REACH, USA, was discussed briefly and plans were presented in outline for the imminent field studies on an auto-destruct syringe proposed by an engineering consultant to USAID. The Group expressed concern that field

studies were being considered for a syringe which had not yet reached production prototype stage with a manufacturer who would be capable of producing them in quantity.

As a general principal and in order to ensure a useful interpretation of field trial results, the Group recommended that field studies should preferably be conducted on samples produced by manufacturers capable and willing to enter into mass production. Nevertheless, it was considered that, if all field trial samples are produced to the US GMP code and sterilization was verified to FDA standards, the minimum requirements for field studies would have been met.

It was agreed that the principal aim of such studies is to estimate the impact, relative to systems already using disposables, of introducing new injection technologies into the EPI in terms of:

- additional training required,
- additional burden on logistics and cold chain,
- marginal extra cost.

Nevertheless, it was felt that longer term monitoring would be needed to see strategic programme management problems and opportunities inherent in the new injection technologies.

ANNEX

EVALUATION OF INJECTION TECHNOLOGIES
Informal meeting, Geneva, 23/24 July 1987
Expanded Programme on Immunization

Summary Report

1. Background and objectives:

Disposable syringes are frequently demanded by countries implementing the Expanded Programme on Immunization. In order to minimize the risk of these syringes being reused, WHO and UNICEF have solicited industry and inventors worldwide for concepts and proposals regarding an "auto-destruct" syringe, useable only once. In a related initiative, USAID through their consulting engineers Programme for Appropriate Technology in Health (PATH) USA, have solicited industry for a similar non-reusable injection device which is pre-filled with a single dose of vaccine or other injectable).

Submissions from industry in response to both these solicitations were gathered together and summarised under a standard format for consideration of a group consisting of eight evaluators and nine observers having the following range of expertise:

- tooling design for disposable syringe manufacture,
- vaccine manufacture,
- bio-engineering,
- senior and mid-level EPI management,
- infection control,
- health technology research and development,
- cold chain logistics.

The objectives of the meeting were as follows:

- To identify the technologies which merit encouragement by the Agencies.
- To identify the features or components of otherwise unsatisfactory technologies which merit further negotiation with the inventors to promote their incorporation into future products.

The provisional terms of reference for the evaluators are listed in Annex 1. Jet injectors will be considered at a future meeting of the group.

2. Method of evaluation:

A total of 35 submissions were received for consideration of the group falling into the following main categories:

- Auto-destruct syringes.
- Pre-filled, single dose devices.
- Other relevant components.

These categories were further sub-divided in advance of the meeting into sub-categories according to the main feature preventing reuse of the device after delivery of a single dose.

The evaluators were introduced to the submissions within each sub-category and invited to discuss the general advantages and disadvantages of the category as a whole before examining each submission.

Evaluation of the individual submissions was conducted with the help of a standard checklist which appears in Annex 2. The group reviewed each submission in a category in turn, then discussed all submissions in that category as a whole and finally returned to each submission to draft their comments.

3. Results:

The evaluation group's opinion of the state of advancement of the concepts which were submitted is summarised for each of the categories in Figure 1.

Figure 1: Injection Technologies Reviewed 23/24 July

CATEGORY/Concept	Number of submissions	Breakdown of submissions by state of development					
		A	B	C	D	E	F
SELF DESTRUCT SYRINGES							
Trapped plunger	7	4	0	1	1	1	0
Destroyed piston seal	3	3	0	0	0	0	0
Break-away plunger	1	1	0	0	0	0	0
Single-direction plunger	3	1	0	0	1	1	0
Trapped plunger handle	3	3	0	0	0	0	0
Blocked fluid passage	1	0	0	1	0	0	0
PRE-FILLED INJECTORS							
Self-contained injection devices							
Trapped plunger	1	1	0	0	0	0	0
Break-away plunger	1	1	0	0	0	0	0
Collapsible pouch	3	0	2	0	0	1	0
Snap closure	1	0	1	0	0	0	0
Disposable needle/reservoir with re-useable injector components							
Punctured bubble	1	0	1	0	0	0	0
Blocked fluid passage	1	0	0	1	0	0	0
Floating piston	3	1	1	0	1	0	0
Collapsible pouch	1	0	1	0	0	0	0
Punctured bubble	1	0	0	1	0	0	0
OTHER RELEVANT COMPONENTS *	4	2	1	1	0	0	0

A = Concept re-design

B = Modify concept and re-submit

C = Component or compatibility R&D required

D = Submit prototype for evaluation

E = Limited manufacture for trial

F = Scale manufacture for routine use

* = Reviewed after the meeting

4. Discussion:

The first questions from managers of the EPI regarding the outcome of this meeting will concern the availability and cost of the new disposable injection technology. It appears today that the auto-destruct syringe will be available sooner than the pre-filled injector and that both technologies will be significantly more costly, both in direct and indirect costs, than sterilization of re-useable equipment.

Self-destruct syringes:

Two self-destruct syringe concepts are now considered ready for limited scale manufacture and field trial, one concept from industry and one from an inventor. It is hoped that field trials can be conducted on both technologies by the end of 1987 and that other concepts will reach the same stage in the first quarter of 1988. Volume production would then be possible by the end of 1988 for more than one manufacturer.

Unit cost estimates for these two self-destruct syringes vary from 6 to 15 cents US representing an increase of at least one third in the cost of a disposable needle and syringe and at least five times higher than the cost of re-usable equipment.

The most common technical problem with the remaining self-destruct syringe concepts was that they demanded voluntary action on the part of the user to render them non-reuseable. They also did not take into account mis-use or minor tampering by the user to make them re-useable. These problems may have been related in part to misinterpretation of the WHO Standard Performance Specification for self-destruct syringes. This specification is now being revised to be more explicit on these points.

Complexity of design or operation was another frequent problem identified by the evaluation group. The most satisfactory solutions are those that added the least number of components to the standard disposable syringe.

All self-destruct syringe concepts so far received will require introductory training of the user, but some concepts are far closer to current injection technique than others. The field trial will take careful note of the extent of training needed and this will be used as an important criterion for the acceptance or rejection of a technology, even at this stage of advanced development.

Pre-filled injectors:

All except two pre-filled injection devices require some research and development to reach a stage when prototypes could be filled with vaccine and used. Neither of the most advanced pre-filled devices have to date actually been filled with vaccine by vaccine manufacturers using routine filling machinery, but for liquid vaccines such as tetanus toxoid and DPT the technical problem is generally considered to be small.

Although several concepts offered the facility to store and reconstitute lyophilised vaccine in single containers, vaccine would have to be freeze dried in bulk and measured as a powder into these containers. Although reportedly implemented in the pharmaceutical industry, this method of filling has not yet been accepted by vaccine manufacturers.

The most advanced pre-filled devices could reach field trials early in 1988 using liquid vaccine only; probably tetanus toxoid vaccine. Other concepts, with potentially important advantages over the two which are the most advanced, will be developed and their progress reviewed by WHO in November 1987. There appear to be areas of over-lapping research and development needs common to similar and different concepts. These will be studied and efforts made to ensure that common research (for example materials compatibility) is conducted only once and made publicly available.

Technically, the pre-filled injection devices fell into two groups; those which were self contained disposable injection devices and those which comprised disposable needle and vaccine reservoirs with re-useable injector devices. The main advantage of the self-contained devices appeared to be their lack of dependance on other equipment while, on the other hand, the re-useable injectors appear to offer less costly disposable vaccine packing occupying less storage space.

Storage volume will be a critical issue for all pre-filled devices which need to be refrigerated in the cold chain. Current estimates predict that six times more refrigerated space will be needed for single dose pre-filled devices than for the conventional multi-dose vials. The indirect costs of adopting pre-filled devices are being studied and will be reviewed at the next informal meeting on injection technologies.

A majority of the pre-filled devices, particularly in the group with re-useable injector devices, were re-useable if re-filling is conducted from a pressurised vaccine vial. Some devices could be easily tampered with to enable them to be refilled by aspiration from a vial. These points of performance will need to be improved before further development is worthwhile.

Finally, the evaluation group expressed concern regarding the accuracy of the vaccine dose (0.475-0.525ml was mentioned as a maximum tolerance for Pertussis vaccine) when delivered by direct pressure of the fingers from self-contained injection devices. This appeared to favour design solutions in which a standard pressure was imposed over a standard part of the surface area of the vaccine reservoir. This criterion will be important in the laboratory verification of prototypes before limited production for field trial can begin.

The evaluation group was unable, due to lack of time, to give specific attention to the "other relevant components" which comprised three anti-stick concepts and a needle assembly. Several discussions took place, however, on the concept of protection of the user and others from accidental wounding by needle. It was concluded that until automatic anti-stick mechanisms appear to be affordable as well as feasible, WHO will specify this level of protection as desirable but not mandatory. However, WHO will specify fixed, retractable or destructable needles and will not accept removable needles. Attention will be focussed instead on disposal systems including containers into which syringes and needles can be thrown after use (and, if necessary carried to a different site for final destruction).

APPENDIX 1 TO ANNEX

TERMS OF REFERENCE FOR THE EVALUATING GROUP

1. Briefly review the main categories of injection device and advise on the relevance of each for EPI. Main categories include:

- Auto-destruct Syringes (direct replacement for standard disposable syringes).
- Pre-filled Single Dose Devices
 - Self-contained injection systems.
 - Disposable reservoir/needle with reusable components.
- Jet Injectors
 - High workload injector.
 - Low workload injector.

NOTE: Jet injectors will be considered by the evaluation group at a later date.

Other Relevant Components

2. Within each category of device, the submissions will be grouped according to the auto-destruct principle employed: for example,

- Devices with piston traps
- Devices which block the passage of fluid after a single use.

Review these general design approaches and comment upon their relative advantages and disadvantages.

3. Within each auto-destruct principle, review each submission (specific concept proposal). Evaluate its general suitability, the next technical steps to be taken, appropriate checkpoints, and the need for further information or review. To the extent possible, based on available information, all recommendations should take into account the following issues:

- a) Compliance with performance specifications.
- b) Risk of cross-infection or accidental needle-stick.
- c) Technical feasibility, device manufacturing, vaccine filling.
- d) Logistical considerations, transport and storage.
- e) Practical training issues; extent of training required.
- f) Cultural considerations.
- g) Issues of national self-sufficiency (e.g potential for local production)

- h) Economic considerations in the short and the long term, taking into consideration the probable foreign and local costs of a) packaged vaccine, b) cold chain, c) the injection system, d) sterilization, e) training, f) disposal and safety.
 - i) Period of time required for implementation.
- 4. The submissions should be scored according to the evaluation matrix provided, after giving further consideration to criteria listed on the matrix form and the weighting accorded to each criterion (scoring to be conducted without reference to the stage of development of the technology).
- 5. Review submissions in the light of their scores and their stages of development. Make recommendations that would address the need for safe EPI injection technologies at the earliest possible time.

APPENDIX 2 TO ANNEX
EVALUATION CHECKLIST

A. PERFORMANCE

Self destruct

The extent to which the syringe barrel and the needle cannot be reused in any way which poses a health risk after one single filling and emptying cycle, without mechanical modification.

Anti-stick

The extent to which the needle becomes automatically and permanently protected from causing a health risk.

Ease of disposal

Ease with which the device can be destroyed without health and environmental hazard.

Volume control

Degree of judgement required to deliver proper dose.

Tamper-proofing

Degree to which the design of the device inhibits mechanical modification for uses which pose a health hazard.

Low need for other equipment and supplies

The extent to which the device can be used without dependence on any other materials.

Universal application

Applicability to all of the EPI injectable vaccines. 0=No, 10=Yes

Protection of vaccine

The extent to which a vaccine is completely protected in pre-filled devices from outside environmental contamination.

Simplicity of design

Design standards which promote straightforward manufacture and low unit cost.

B. COST/EASE OF MANUFACTURING

Availability and cost of key materials

Availability of the materials from a number of sources at a competitive cost.

Compatibility with current manufacturing processes

Extent to which existing device manufacturing processes and machinery can be utilised or adapted without difficulty.

Compatibility with current finished goods processes

Extent to which existing vaccine filling processes and machinery can be utilised or adapted without difficulty.

High degree of current industrial interest

Indications of commercial interest or state of advancement which suggest a high probability of success.

Suitability for local manufacturing in EPI countries

C. COST/EASE OF INTRODUCTION

Low cold storage space needs

The extent to which the pre-filled devices can be accommodated within the refrigerated storage space and transport available in the cold chain today.

Low vaccine wastage

Obviousness of use (training burden)

Similarity of use in comparison to standard syringe and therefore an assessment of the extent of training required.

Suitability for commercial markets

The strength of other commercial markets which would provide useful economies of scale or other advantages.

Logistics (other than cold storage)

Low fragility, low weight and low volume of shipping and storage.

Use with existing vaccine supplies

Ability of injector to be used with existing multi-dose vaccine presentation.

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