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Rapid Communication

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Maximizing number of doses drawn from multi-dose COVID-19 vaccines by minimizing dead-volume

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The COVID-19 pandemic constitutes an unprecedented challenge to health care systems and societies worldwide. On 21 December 2020, the highly effective Pfizer–BioNTech COVID-19 vaccine was authorized in Europe, bringing big hopes for overcoming the pandemic.[1] However, there are concerns about delayed availability of sufficient vaccine doses, forcing to prioritize target populations.[2] Vaccination with the Pfizer–BioNTech COVID-19 vaccine consists of two doses (0.3 ml each) administered intramuscularly, 3 weeks apart. Each vial (2.25 ml theorical and 2.27 ml actual volume after dilution) meet the requirements of the European Pharmacopoeia allowing to obtain five doses using a syringe of a capacity not exceeding three times the volume to be measured and fitted with a 21-G needle not less than 2.5 cm in length.[3] On 8 January 2021, European Medicines Agency announced that six doses could be extracted from a single vial using low dead-volume syringes and/or needles; i.e. no more than 35 µl for the syringe–needle combination.[4] To date, no study has been carried out to propose recommendations on the use of adapted equipment. Here, we report the dead-volume of different syringe–needle combinations in order to inform such debate by relevant medical devices data.

Based on the standard method NF-EN ISO 7886-1,[5] the volume administered by tuberculin syringes, the dead-volume of several syringe–needle combinations and the number of doses extractable from Pfizer–BioNTech COVID-19 vaccine vials by different syringe–needle combination were measured using Sartorius ME254S-OCE analytical balance as shown in Figure 1. Although there are many brands of syringes and needles, including syringes with integrated hubless needles where the needle retracts after use, we have focused on the main syringes and needles available for vaccination campaigns in France. Firstly, we found that the same syringe on different needles did not give the same dead-volume (Figure 1a) highlighting the importance of the dead-volume at the needle hub. This finding suggests that syringe–needle combination can't be determined in a random way for the purpose of extracting additional doses. Secondly, tuberculin syringes do not all withdraw the same volume at the 0.3-ml graduation, some withdrawing up to 0.32 ml (Figure 1b). Consequently, an unnecessary volume may be withdrawn in addition to the dead-volume of the syringe–needle combination, compromising the chances of extracting a sixth dose from a vial. Lastly, we showed that the needles crimped onto the syringe offer the lowest dead-volume (i.e. 1.8 ± 0.6 µl for the needle crimped onto the syringe 25 G [Hunan Pingan Medical Technology] and 4.8 ± 1.4 µl for the needle crimped onto the syringe 23G SOL-M [reference 181 023]), allowing to extract up to seven doses from a single vial (Figure 1a and c). Interestingly, feedback from the field showed that extracting the seven doses was feasible without slowing down the patient flow, although experienced vaccinators did it more efficiently.

These data have the potential to optimize limited vaccine resources available in this unprecedented global health context as additional doses may increase the number of people vaccinated. Moreover, these dead-volume data can be extrapolated to other multi-dose COVID-19 vaccines and may allow the use of additional doses by taking advantage of overfilling. Although

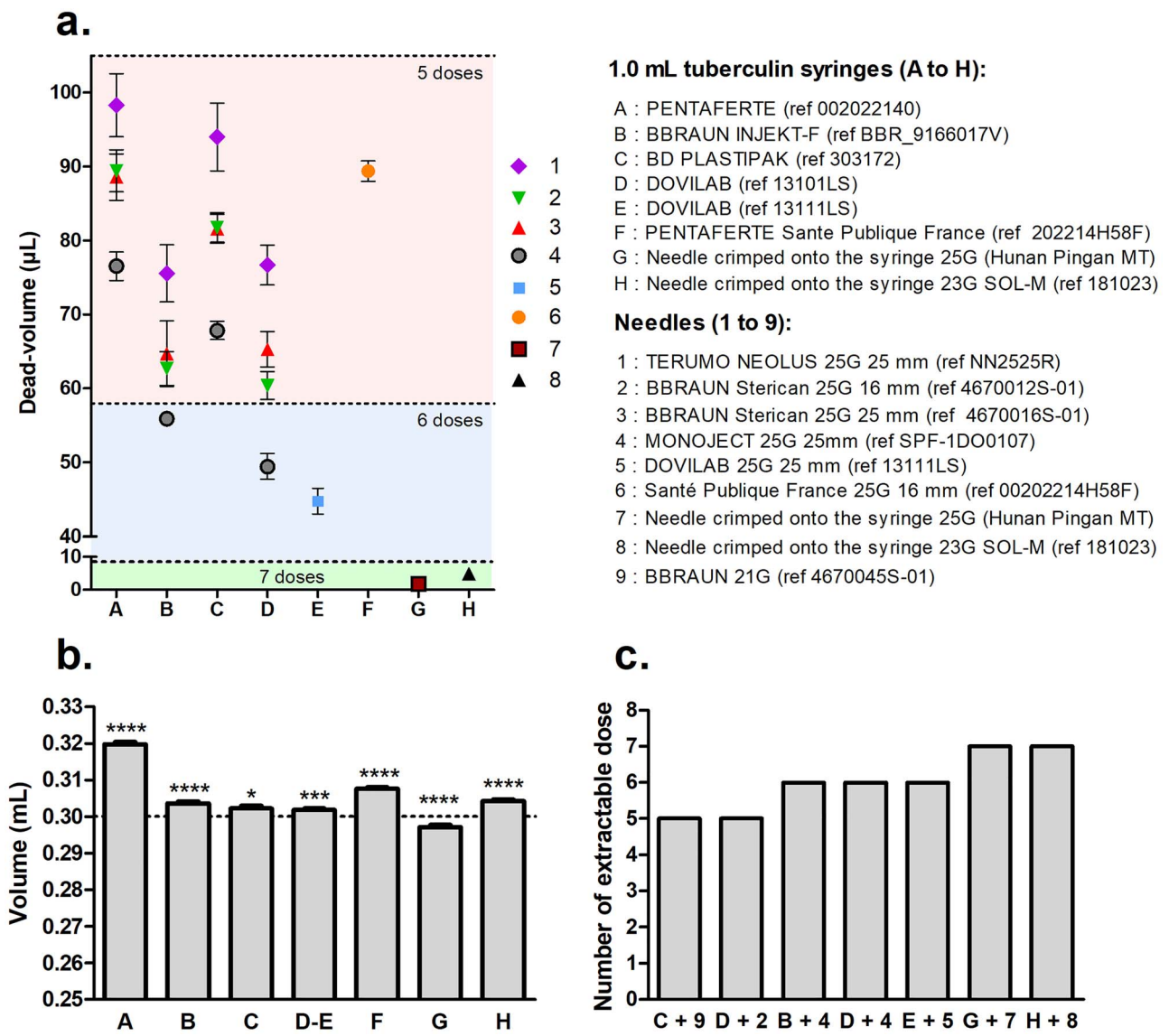

Figure 1. (a) Dead-volumes (µl) of different syringe—needle combinations measured according to standard method NF-EN ISO 7886-1. (b) Actual volume administered by different syringes at 0.3-ml graduation. (c) Number of extractable dose from Pfizer–BioNTech COVID-19 vaccine vials according to different syringe–needle combinations. The data are quoted as the mean ± standard error of mean from at least 5 (a), 50 (b) or 3 (c) independent and blinded measurements. The differences with the theoretical value (0.3 ml) were probed using *t*-test. $^{****}P < 0.0001$; $^{***}P < 0.001$; $^{*}P < 0.05$: volume of one syringe compared with the theoretical volume withdrawn (0.3 ml)

we show that the extraction of extradoses can be achieved with two references of needle crimped onto the syringe, this does not exclude that other references can also allow this maximization of the number of dose extracted from multi-dose COVID-19 vaccines. Achieving timely completion of vaccination campaigns in the high-risk people on a global scale could help prevent the vast majority of COVID-19 deaths well before herd immunity on the level of entire populations is achieved. Thus, every effort should be made in the local context to maximize yield by researching available options and training vaccinators to use the best local available option with maximum efficacy. Considering many countries are still facing the second wave of the pandemic, we urgently recommend, based on the evidence, the use of needles crimped onto the syringe for the administration of COVID-19 vaccines.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

None declared.

Contribution statements

All authors have contributed equally.

References

1. Polack FP, Thomas SJ, Kitchin N *et al*. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383**:2603–15.
2. Mills MC, Salisbury D. The challenges of distributing COVID-19 vaccinations. *EClinicalMedicine* 2021; **31**:100674.
3. European Pharmacopoeia (Ph. Eur) 10th Edition|EDQM-European Directorate for the Quality of Medicines. https://www.edqm.eu/en/european-pharmacopoeia-ph-eur-10th-edition (21 February 2021, date last accessed).
4. CZARSKA-THORLEY D. Extra dose from vials of Comirnaty COVID-19 vaccine. *Eur Med Agency*. 2021; published online Jan 8. https://www.ema.europa.eu/en/news/extra-dose-vials-comirnaty-covid-19-vaccine (21 February 2021, date last accessed).
5. ISO 7886-1 (2017). Sterile hypodermic syringes for single use. Part 1: Syringes for manual use. https://www.iso.org/standard/64790.html (21 February 2021, date last accessed).